Entered as second-class matter at the Post Office at Philadelphia, Pa., under the Act of March 3, 1879.

AMERICAN JOURNAL OF PHARMACY

A RECORD OF THE PROGRESS OF PHARMACY AND THE ALLIED SCIENCES

VOL. 93 SEPTEMBER, 1921 No. 9

CONTENTS

Price $3.00 per Annum in Advance. Foreign Postage, 25 Cents Extra.
Single Numbers, 30 Cents. Back Numbers, 50 Cents.

Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917. Authorized February 15, 1920.

PUBLISHED MONTHLY BY THE
PHILADELPHIA COLLEGE OF PHARMACY and SCIENCE
145 North Tenth Street, Philadelphia

THE AMERICAN
JOURNAL OF PHARMACY

VOL. 93. SEPTEMBER, 1921. No. 9.

EDITORIAL

THE ALCOHOL PROBLEM.

The Prohibition Amendment constitutes one of the most radical modifications of general law that the world has ever experienced. The extinction of slavery was a violent change, but the slave area was a comparatively small part of the United States, and the other great nations had long since abandoned the system and even placed it under active condemnation. The use and abuse of alcoholic beverages go back to the remotest periods of written history. They have been always associated with the joyous side of life, and have also been regarded as valuable therapeutic agents. The Amendment practically cuts out all these relations, for as interpreted by the Act of Congress the proportion of alcohol permissible is so far below that in the normal beverages as to be regarded by the mass of the people as without value.

Undoubtedly this remarkable legislation has been largely due to the persistent refusal of the liquor interests to control in any way the objectionable features of the traffic. Just as the slave-lords, in the first half of the nineteenth century, not only refused to mitigate the cruelties of slave life, but demanded further extension of it and unlimited privileges, so the liquor interests, making no effort to reduce the abuses of the saloon, selling without hesitation to unlicensed places and in many other ways showing an indifference to law and order finally aroused so much opposition that, as in the case of slavery, the whole institution was swept away, without regard to the economic effects or abstract legal principles involved.

In the present state of affairs, the position of the practicing pharmacist is serious. In proportion as law enforcement eliminates the saloon or throws it into alleys and by-ways, the drug store is

liable to become the substitute, and it behooves all who have the maintenance of pharmaceutic ethics at heart to use every effort to counteract this tendency. Black sheep there will be in spite of all teaching and example, but the faculties of our pharmaceutical colleges and the controllers of pharmaceutic organization must preach in and out of season the duties of the retail pharmacists with no uncertain voice. The question is, of course, seriously complicated by the general opinion that alcoholic beverages have a medicinal value, and by a somewhat widespread opinion that they have also a food value. It cannot be denied that moderate amounts of alcohol are consumed in the animal system with production of energy, but it can be easily shown that such energy is more expensive than that from any common article of diet. The view that a moderate amount of alcohol has a so-called "protein-sparing" power never had any satisfactory experimental basis, and does not now form any part of scientific opinion in this field.

A phase of the alcohol question that needs active discussion is that of adulteration. Habits die hard, and those addicted to the use of alcohol, or lenient in regard to its use in others, are found very frequently repeating the shibboleth that if only "pure" liquors would be sold the evils of intoxication would be materially abated. The widespread notion that poisonous substances are frequently added to beverages, especially those sold in violation of law, finds no support in the experiences of chemists. It is true that, lately, a good many cases of adulteration with methanol (or even complete substitution of this substance) have been reported, but such practices lead usually to the just punishment of those who drink the liquor, inasmuch as such admixture is generally found only in liquors sold in violation of the law. The dangerous ingredient in alcoholic beverages is the alcohol; the stories of the use of strychnin in beer and of cocculus berries in other liquors are like the stories of arsenic and opium in cigarettes, sand in sugar or chalk in milk, the invention of newspaper reporters.

The value of alcoholic beverages in treatment of disease is as yet an unsolved problem. It cannot be doubted that a substance that has such prompt and toxic effects as alcohol must have applications in rational therapeutics, but alcohol differs from almost all other remedial agents in the gustatory characters of its commercial forms. If the only available form was the silent spirit, that is, the almost

flavorless mixture of ethyl hydroxide and water, it is probable that alcoholic excess would be much less frequent, although it is true that many persons have such depraved taste that even disagreeable mixtures will be drunk for the sake of the intoxicating effects. It is along the line of this medicinal use that the greatest danger lies, and it is a danger especially affecting the retail druggist, who is constantly and unavoidably brought in contact with those who resort to self-medication. Unless the attitude of the mass of druggists is held in uncompromising antagonism to any deference to those who seek to secure alcoholic beverages under the excuse of illness, there is grave danger that the corrupting influence of the saloon will be transmitted to the drug store, and the latter become an outpost in the underworld.

HENRY LEFFMANN.

ORIGINAL PAPERS

VISITING OLD FRIENDS.

A BRIEF ACCOUNT OF A SEPTEMBER BOTANIZING TRIP IN SOUTH JERSEY.

By CHARLES H. LAWALL, PH. M.

A professor of pharmacy and his assistant, an ex-president of the American Pharmaceutical Association and two ex-presidents of the Philadelphia local branch thereof, a former presiding officer of the Pennsylvania Pharmaceutical Association, the dean of a pharmacy college, a hospital pharmacist and assistant pathologist, an ex-chairman and present member of the U. S. P. Revision Committee, a member of the A. Ph. A. Committee on Druggists' Recipe Book, a member of the National Formulary Revision Committee, an instructor in pharmaceutical arithmetic, two members of the American Chemical Society, a member of the Philadelphia Botanical Club and one of the Pennsylvania Botanical Society—all these fared forth one fine day in early September to renew their acquaintance with the flora of the coastal strip and adjacent mainland in the neighborhood of Great Egg Harbor Bay, New Jersey.

TYPICAL CEDARS ALONG A WIND-SWEPT WASTE.

WATER LILIES.

WHERE TIDES AND MEADOWS MEET.

WILD CARROTS IN AUTUMN.

The conveyance used was a small touring car, of which the whole party occupied the front seat. Impossible? Not at all, for you see, there were only two individuals, after all. In the rear seat and on the floor of the car were piled a vasculum, several cameras, two pairs of rubber boots, a large vase and several handbooks on systematic botany.

SEASIDE GOLDEN ROD.

The sea breeze blowing on their backs had a tang of autumn in it, although the sun was warm overhead. Away across the meadows and marshes were many plants recognizable at a distance. Clumps of bayberry and groundsel here and there relieve the flat monotony of the landscape. On the borders of the woods lining the western side of the coastal strip were rows and thickets of staghorn

and upland sumach, with now and then a sassafras standing out, showing promise of reds and yellows to come when the leaves are frost touched.

The sea rocket sprawled over the level sandy places and the deeper green of patches of beach heather carried the thought back to early summer when the golden, insect-laden blooms vie with the purple of the lupine in catching the eye of the speeding wayfarer along miles of pine barren roads.

The seaside golden rod, almost bush-like in size and growth was seen on every side.

The procumbent sensitive plant with its yellow flowers and irritable leaves bordered the foot paths, while the Indian mallow and clotbur, coarse-leaved and despised by man and beast alike, were everywhere abundant.

The omnipresent bouncing bet, the common pepper grass, the yellow flowered mustard, the yarrow with its delicate fern-like foliage, the smartweed and an occasional daisy, were familiar friends whose absence would probably make them more conspicuous than does their presence, they are so homely and common. In this recital of the commonplace must not be forgotten the diminutive black nightshade everywhere underfoot, nor the ungainly evening primrose, an ugly plant with a pretty name.

In the open spaces of the meadows could be seen the saltworts and samphires, which in October and November flood the scene with a crimson haze as one looks toward the horizon. In among the waving marsh grass were clumps of sea lavender, sometimes called marsh rosemary, which was at one time official in the U. S. P., but which has long since been discarded from medical practice. A bunch of these plants makes a fine winter bouquet.

Each little tidewater thoroughfare is outlined by the tall grasses bordering its course, and the pattern of their lines of deeper green is conspicuous and curiously intricate and attractive, reminding one of a gigantic picture puzzle.

As soon as the mainland is reached other interesting and familiar plants are encountered. The ubiquitous poke and the dreaded poison ivy greet one from almost every fence corner. This selective distribution is ornithological in its etiology. The choke cherry also is frequently found in similar situations for the same reason.

Back of the fences, along the edges of cultivated fields are tangled patches of wild blackberry and dewberry, with wild strawberry plants, now long since the fruiting stage, peeping up between. The wild rose shows by its abundant red hips, the glory of the bloom that has passed with early summer. The beach plum, low and straggling, the haven of nesting birds, is now hung with purple fruits of honied sweetness with an attractively bitter after tang. The Virginia creeper, its older leaves already changing to scarlet, clambers over fence and tree, showing marked contrast to the deep mossy green of the cat brier, which loves the edges of thickets and deep, cool woods.

Leisurely traversing the country by the smaller wood roads, many interesting trees and shrubs are noted. The scrub pine is predominant in certain areas, accompanied by the ubiquitous swamp and blackjack oaks. The foreground is of bracken, with sensitive fern bordering the roads. Against the skyline as we leave the marshes are rows of cedars with their wind-twisted branches, distorted but defiant, exemplifying adaptability and stubbornness at the same time, often assuming grotesque shapes or reminding one of all kinds of unrelated things.

In the roadside thickets on the edges of the woods, the sweet pepper bush reaches out its fragrant white flower clusters. Here and there stands up a button bush with its globular flower heads, as if in martial salute. An occasional glimpse of the glossy, deep green, spiny leaves of the holly remind us of Yuletide decorations and seem strangely out of place. Its closest relative, the black alder, too, with its berries in close-clustered whorls, now beginning to turn red, is a reminder of Christmas wreaths.

Here and there a glimpse of a single scarlet branch on a tree yet robed in living green, calls attention to the two trees that even in midsummer anticipate the brilliancy of their autumn foliage. They are the sour gum with its oval, and the sweet gum with its star-shaped leaves. Dogwoods, huckleberries and blueberries, laurels, both the calico bush and the diminutive sheep laurel, and an occasional viburnum, are observed as we go further inland.

As we pass a marshy woods, the silvery, silky undersides of the swamp magnolia leaves are visible in all directions, and one longs for the fragrance that surrounds the spot in early June, when their tightly wrapped, cream white buds shed a woodsy odor, which often perfumes the air for miles at a stretch. Here we pass a thicket, in the

midst of which the tall and stately Turk's cap lily, having just completed flowering, thrusts its fruit up conspicuously, while along the very edge of the road the day lily, too, is noted in the fruiting stage. Here a rag weed flaunts its hay fever-compelling blooms and there the coarse sow thistle stands up in vulgar arrogance.

The tall wool grass beckons us to take it along for a decoration lasting all the year, while the beggar's ticks and tickseed dare one to venture within their reach.

An old, neglected clearing, once a cultivated field, affords a rich botanical repast. Here is the brilliant bloom of the orange milkweed, almost recumbent, while quite near and much higher are the purple globular flower clusters of the common milkweed, already beginning to shed their silky plumes from earlier borne flowers. Underfoot is the self-heal, while its distant relative, the horsemint shows in scattered clumps of purplish brown.

The delicate purple Gerardia monopolizes the open spaces, while just inside the dry woods, at the edge of the clearing, is seen its yellow-flowered cousin, the downy false foxglove. Along the hedgerow is a purple-flowered spirea, and a patch of tansy and a mulberry tree are evidences of a former habitation, of which the ruins of an old cellar wall give confirmation. Here, too, is blue vervain and scattered about in profusion may be seen black-eyed Susans, wild sunflowers and boneset.

Golden rod and asters are plentiful both as to numbers and variety. One of the conspicuous features of a cleared patch of this sort are the clumps of wild indigo, almost as regular in form as though a landscape gardener had trimmed them, with the blue-green, characteristic foliage which defies all effort at preservation in a herbarium.

Then, too, there are the clovers, the red and white, and sometimes the Alsike, usually seen in isolated patches. The silky soft heads of the rabbit clover, also known as old field clover, from its tendency to spread where cultivation has been abandoned, give a grey mistiness to the vista, on looking across the level stretches, that is peculiarly attractive.

Patches of vetch in riotous exuberance catch the eye and in all directions we can see the lacy blooms of the wild carrot, slightly convex in the early stages, but reversing this form as the flowers pass maturity, the final fruiting clusters looking like a bird's nest on the end of a stem.

Groups of fireweed, ugly and persistent, strike a discordant note now and then which is relieved by its silky gray competitor, life everlasting, so often used for filling fragrant pillows and cushions for tired heads. On one side is a dry woods, where by walking but a few steps from the road is found the three wintergreens, the *Gaultheria* or fragrant, the *Chimaphila* or spotted, and the *Pyrola* or shin-leaf. Here, too, is found the Mitchella or teaberry, also called partridge berry, and an occasional rattlesnake plantain, which belongs to the orchid family.

Over to the right is a deeper green and greater luxuriance of foliage which promises much, if, as we hope, it is a cedar water pond or a cranberry bog. On the edge we find iron weed and Joe-pye vying for supremacy. As we approach nearer to the water the lush damp grass, we see, is dotted with many colors of flowers loving wet places. Here we find the deer grass or meadow beauty alongside the blue-eyed grass, neither of them, however, being really grasses. The cross-leaved or marsh milkwort, with its purple flower heads is intermingled with the orange milkwort, sometimes known as the wild bachelor's button. The marsh pink or Sabbatia here shows its starry pink flowers with their contrasting yellow centers.

The common lobelia, known as Indian tobacco, is found here and almost at the water's edge we find the wild cranberry plant, with flowers and fruit both present at the same time. Most persons have an idea that cranberries grow on bushes and are surprised when they first become acquainted with the plant as it grows and see its diminutive size as compared with its fruits.

Now we reach an opening that leads to the water's edge and looking across the amber transparency of the cedar pool, dotted with islet-like clumps, we are confronted with a scene of unusual beauty. Along the edge are tall, graceful plants of meadow rue, the beauty of whose finely divided foliage is unmatched by any other plant of its size. The spotted hemlock rises to a height of five or six feet with its umbels of white flowers borne on purple stalks. The button snakeroot or rattlesnake master, with its steel blue flower clusters and feathery foliage is striking in its individuality.

Lower down the cardinal lobelia makes a bright spot of contrast with the deep blue giant lobelia, which accompanies, and the white waxy blossoms of the arrowhead are again contrasted with

the bright blue of the pickerel weed now passing into the chaffy, brown fruiting stage. The white, button-like tops of the pipeworts remind us of a collection of hatpins stuck in the marsh at various angles. The yellow blossoms of the spatter docks look vulgar and common when contrasted with the blooms of the white fragrant water lilies lying outspread in graceful symmetry of both leaf and flower. The sword-like leaves of the several species of iris which had bloomed some time since, are in close resemblance to the foliage of the bulrushes or cat tails which are now approaching maturity.

Back in the swampy edges are clusters of plants of the cotton grass, each stalk looking for all the world like a bunny's tail tied on the end of a stick. At our feet, half submerged, lie the deep blue-green, large velvety leaves of the golden club, which bloomed in early summer. Just at the water's edge is a pitcher plant with its curious, pouch-shaped leaves, and its nodding red and yellow, button-shaped flower. Lower down and only seen when searched for are the sundews, both round and thread-leaved, and the delicate yellow-flowered bladderwort, buoyed up by its balloon-like foliage.

After such a treat we are well content to turn our course homeward, for we have stored in our memories pleasant scenes and have a feeling down in our hearts that we have been close indeed to nature.

"What is the score?" says the professor to his assistant. "One hundred and eleven," is the answer, for copious notes have been taken as we sped along. "Here is another one," shout both the pathologist and the botanist, just as home is reached on the sandy spit, and there, forgotten and overlooked, in the front yard stands a fine specimen of that alien immigrant, long since naturalized, the Jimson weed.

"And here is one for a finale," says the professor as he steps upon a specimen of the sandbur, so appropriately named *cenchrus tribuloides*.

"Are you going to write this up?" asked the instructor in pharmaceutical arithmetic. "If so, which book are you going to follow for the botanical names, Gray or Britton & Brown?" "Forget the botanical names," answered the Dean. "This was purely a pleasure trip, not an educational one."

DETERMINATION OF CAMPHOR IN CAMPHORATED OILS.

By D. A. Wallace and S. B. Plummer.

The object of this investigation was to determine the experimental conditions for the correct estimation of camphor, dissolved in cottonseed, olive, peanut and sesame oil, by the methods of, firstly, volatalizing the camphor; secondly, by the use of a saccharimeter with a bichromate cell. These oils were selected as being those specified by the British or United States Pharmacopœia.

The first method consists in heating a known weight of camphorated oil at 120° C. until the camphor has volatalized,[1] the loss in weight, after allowing for the change in weight of the oil, representing the amount of camphor contained in the sample. The time necessary for complete evaporation at this temperature was determined. Likewise an examination of the oils before and after heating, with and without camphor was made, to find what changes in such physical and chemical properties of the oils, as refractive index, iodine absorption and saponification values had taken place. Likewise the change in weight on heating the oils alone was measured.

Japanese camphor was resublimed many times in ordinary desiccators placed on a warm electric plate, until further sublimation failed to change its melting point, the camphor so obtained was used throughout as being sufficiently pure for the purpose.

In Table I are given the physical and chemical constants of the oils employed; the specific gravities were determined by the Westphal balance at 15° C., the refractive indicies were determined by both the Zeiss-Butyro and Abbe refractometers at 40° C., the saponification values were made according to Köttestorfer's process and the iodine numbers by Wijs' method. The values recorded are the average of two or more determinations.

TABLE I.

Oil	*S. G.*	*Butyro-Refractometer.*	*Abbe Ref'r.*	*Saponification Value.*	*Iodine Number*
Cottonseed	0.924	57.7	1.4648	198.7	110.4
Peanut	0.918	56.3	1.4639	192.8	97.8
Olive	0.916	54.0	1.4622	192.7	84.0
Sesame	0.923	58.5	1.4652	193.1	104.6

[1] Allen's Comm. Organic Chemistry, Vol. 4, p. 199.

From these determinations all of the oils would appear to be commercially pure, the cottonseed oil gave a high saponification value, whilst the refractive index of the olive oil is slightly below normal.

Standard solutions of camphor were then prepared, eighty grams of the various oils were weighed into glass stoppered bottles and exactly twenty grams of camphor added, giving solutions 20 per cent. by weight, as required by the British and United States Pharmacopœia. After the solutions were uniformly mixed, five gram samples of each were weighed, into five centimeter diameter platinum dishes and placed in a Freas oven, previously regulated to 120° C. At the same time four gram samples of each oil were weighed into similar dishes and heated in the same oven. At the end of two hours all the samples were removed from the oven, desiccated for twenty minutes, and weighed. This process was repeated for a third and fourth hour. The weights at the end of the fourth hour were very little different from those at the end of the third, except in the case of cottonseed oil, which was heated for a fifth hour.

The refractive indicies, saponification values and iodine numbers of the oils after being heated both with and without camphor, for five hours in the case of cottonseed, and four hours in the other cases, were then determined, with the following results:

TABLE II.

REFRACTIVE INDICIES (ABBE) AT 40° C.

Oil	*Before Heating*	*Heating with Camphor.*	*Heating without Camphor*
Cottonseed ..	1.4648 (58.3)	1.4680 (63.2)	1.4667 (61.2)
Peanut	1.4639 (56.9)	1.4660 (60.2)	1.4654 (59.2)
Olive	1.4622 (54.3)	1.4631 (55.7)	1.4626 (55.0)
Sesame	1.4652 (58.9)	1.4687 (64.3)	1.4679 (63.1)

The equivalent Butyro refractometer readings are included in brackets. The effect of heating the oils has in every case been to raise quite appreciably the refractive index,[2] a greater effect being produced on the oil when containing dissolved camphor. These values may afford some information for the identification, by means of the refractometer, of these oils after heating to volatilize camphor.

[2] Compare Utz (Chemical Technology & Analysis of Oils, Fats & Waxes, p. 343, V. I).

TABLE III.

SAPONIFICATION VALUES.

Oil	*Before Heating.*	*Heating with Camphor.*	*Heating without Camphor.*
Cottonseed*	198.7	198.8	199.0
Peanut	192.8	193.7	195.0
Olive	192.7	193.3	193.5
Sesame	193.1	194.3	194.0

TABLE IV.

IODINE NUMBERS.

Oil	*Before Heating.*	*Heating with Camphor.*	*Heating without Camphor.*
Cottonseed	110.4	97.4	99.05
Peanut	97.8	85.5	88.4
Olive	84.0	78.5	81.7
Sesame	104.6	97.9	99.7

The saponification values were but little affected by prolonged heating, whilst the change produced in the iodine values, due to probable oxidation of the oils would have to be taken into account in utilizing such determinations for the identification of oils after heating to drive off camphor. Tolman and Munson [3] found the iodine value of peanut oil to fall as low as 77 after prolonged heating.

The following table shows the effect produced by heating five grams of the 20 per cent. camphorated oils and four grams of the oils (Blank Oil), for the number of hours indicated in 5 cm. diameter platinum dishes at 120° C.:

TABLE V.

Oil	*Hours Heated*	*Apparent Loss of Camphor.*	*Blank Oil. Gain Gms.*	*Blank Oil. Gain %*	*Corrected Loss.*	*% Camphor Evaporated.*
Cottonseed	2	0.8885 gms.	0.0065	0.163	0.8950	89.50
	3	0.9743	0.0114	0.285	0.9857	98.57
	4	0.9815	0.0135	0.337	0.9950	99.50
	5	0.9855	0.0142	0.350	0.9997	99.97
Peanut	2	0.8830	0.0086	0.215	0.8916	89.16
	3	0.9827	0.0126	0.315	0.9953	99.53
	4	0.9895	0.0138	0.345	1.0033	100.33*
Olive	2	0.9875	0.0035	0.0875	0.9910	99.10
	3	0.9897	0.0086	0.215	0.9983	99.83
	4	0.9880	0.0108	0.270	0.9988	99.88
Sesame	2	0.9977	0.0006	0.015	0.9983	99.83
	3	1.0017	—0.0010	—0.025	1.0007	100.07*
	4	1.0034	—0.0015	—0.0375	1.0019	100.19*

[3] "Olive Oil and Substitutes," U. S.. Bureau of Chemistry Bulletin No. 77, p. 45, note e.

The values indicated by * are probably accounted for by the oxidation of the oils proceeding faster in presence of camphor than when heated alone. This view is confirmed by the iodine values, above obtained, being smaller for the oils from which camphor had been volatilized than for the oils heated alone for the same length of time; if so, it would follow that the gains recorded under (Blank Oil), representing the increase in weight of the oils due to oxidation on heating the oils alone, are slightly less than should actually be added to the "apparent loss" to give the actual loss.

From these determinations, which have been limited to the examination of one sample of each oil, camphor in camphorated oil may be determined from the loss in weight on heating in platinum dishes at 120° C. for five hours in the case of cottonseed, four hours in the case of peanut and olive, and three hours in the case of sesame oil, after adding 0.35, 0.26, 0.27 and minus 0.042 per cent., respectively, of the four grams of oil taken for the experiments.

OPTICAL ROTATIONS.

The optical rotations of the camphorated oils were determined by a half-shadow, single wedge compensatin saccharimeter, using a nitrogen lamp as source of light. To eliminate, as far as possibe, the difference in the colors of the field of view a cell containing two centimeters thickness of 10 per cent. bichromate solution was placed between the light and illuminating lens. An appreciable difference was noted when observations were made at one time with and at other times without the dichromate cell. The reading recorded are the average of several measurements and are for a 200 mm. tube at 20° C.

TABLE VI.

Oil.	*Rotation of Oil.*	*Rotation of Camphorated Oil*	*Absolute Rotation.*	*Angular Rotation.*	*Angular Rotation for 1% Camphor.*
Cottonseed ..	—0.45° V.	56.6° V.	57.05° V.	19.79 ang.	0.989 ang.
Peanut	—0.1	56.90	57.00	19.72	0.986
Olive	0.2	57.4	57.20	19.82	0.991
Sesame	2.85	59.25	56.40	19.56	0.978

From these results the calculated angular rotation for a 200 mm. tube is about 0.98-0.99 for each per cent. of camphor for solutions of standard pharmacopœial strength.

SUMMARY.

The experimental conditions are given for the determination of camphor in camphorated oil by (1) loss on heating; (2) by the use of a saccharimeter.

The present investigation was undertaken at the suggestion of Dr. R. H. Clark, and was carried out with his co-operation.

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HIGH-LIGHTS IN THE HISTORY OF THE PHILADELPHIA COLLEGE OF PHARMACY.

JOSEPH W. ENGLAND, Ph. M.

Vice-Chairman of Board of Trustees, Philadelphia College of Pharmacy and Science.

The history of the Philadelphia College of Pharmacy—the first college of pharmacy in the New World—covers practically the history of pharmaceutical education in this country. From the time of its institution as the Philadelphia College of Apothecaries in 1821, and its incorporation as the Philadelphia College of Pharmacy in 1822, it has exerted a potential influence in developing pharmaceutical education, initiating many of its most forward steps, while indirectly, through the daily work of its thousands of graduates, it has rendered a nation-wide service for the relief of human suffering and the conservation of public health.

The College was founded by sixty-eight druggists and apothecaries of the City and Liberties of Philadelphia on February 23, 1821, the result being crystallized by the decision of the Board of Trustees of the University of Pennsylvania on February 21, 1821, to institute a course of instruction for students in pharmacy leading to the degree of master of pharmacy, which decision, however distasteful to the druggists and apothecaries, had a certain ground of reasonableness, and aroused their dormant pride and self-respect, compelling them to take action for the protection and advancement of their profession; and I am told by Dr. Edgar Fahs Smith, of the University of Pennsylvania, that "the University-pharmacy-course was never given"—which is to the everlasting credit of that great

institution—although on April 5, 1821, the University did, indeed, proceed so far as to confer the honorary degree of master of pharmacy upon sixteen apothecaries of Philadelphia, the first grant of a pharmaceutical degree in this country.

The College was founded in historic Carpenter's Hall, a building occupied in 1774 by the Provincial Assembly which recommended a general Congress of all the American Colonies, which Congress also met in this hall, and within it inaugurated those measures which, after the perils of the Revolution, terminated so favorably for civil liberty in America and throughout the world; and so, within this hall the "sixty-eight druggists and apothecaries" met and wrote a new declaration of independence: That pharmaceutical education shall be of pharmacists, by pharmacists and for the public welfare.

Prior to 1821, "in this new country with its sparse population and vast territorial extent—its few small but growing cities scattered along the seaboard—the occasion had scarcely arisen to put into practice the obvious educational means fitted to meet these requirements; but now the time had evidently come. Every intelligent druggist and apothecary felt that the instruction which might be suitable for the student preparing himself for the duties of the physician would be only partially fitted for one who was to assume the widely different responsibilities of the drug store and dispensary." (Historical Memoirs of the Philadelphia College of Pharmacy, Edward Parrish, AMER. JOURN. PHARM., 1869-97.)

Furthermore, the founders of the College realized that their responsibilities were not only to provide pharmaceutical education, but also to protect the public against the adulteration and misbranding of drugs; thus, at the second meeting of the College (March 13, 1821), a committee appointed at the first meeting reported that abuses had crept into the drug and apothecary business; instances had occurred of deteriorated drugs being introduced into the shops and valuable remedies in daily use being adulterated and sold of inferior quality and that such abuses were attributable in part "to want of proper pharmacological information on the part of some druggists and apothecaries who vend and of physicians who buy," and it was recommended, with the establishment of the College, that its "attention be constantly directed to the quality of articles brought into the drug market, subjects relating to the business and its objects be

discussed, and information beneficial and instructive to the trade communicated."

It is of interest to note that "the first years of the College were marked by great activity. Committees of inspection were appointed to examine drugs introduced into the market, and to expose adulteration and sophistication. Latin labels were printed, carefully adapted to the officinal standard of nomenclature. Formulas were published for the old English remedies called 'patent medicines,' then very extensively sold, with a view to greater uniformity in their composition and properties; and the absurdly-worked wrappers in which these were enveloped, giving false or exaggerated accounts of their virtues, were measurably superceded by more sensible and truthful 'directions.' Meanwhile, a library was being formed, a cabinet of the specimens collected, and the various improvements in chemistry and pharmacy suggested from time to time were investigated and reported upon" (Edward Parrish).

In this way the College sought to prevent the manufacture and sale of adulterated or misbranded or deleterious drugs and medicines, thereby anticipating in a sense the enactment of the Federal Food and Drugs Act of nearly one hundred years later, but the influence of the College was wholly educational and moral, and no adequate protection was given to the public until the enactment of the Federal Food and Drugs Act of 1906, one of the most righteous laws ever passed by the United State Congress.

And the work so auspiciously begun by the College one hundred years ago has been continued through the century with ever-increasing vigor and efficiency.

The College has achieved its unusual success as an educational institution because it has been built upon the bed-rock of character. The sixty-eight men who instituted the College were mostly members of the Religious Society of Friends, commonly called Quakers, who believed in the homely virtues of modesty, thrift and wisdom, and love of peace and simple honor, and practiced these; men of plain living and high thinking, men of strong and positive opinions, and men of practicality, thoroughness and love of humanity.

And it was this love of humanity, doubtless, that inspired their love of education. As William Penn, the founder of Pennsylvania, wrote: "Friends consider education as a right and a privilege, to the end that the poor as well as the rich may be instructed in good and commendable learning, which is to be preferred before wealth."

The aim of the Quaker founders of the College—and their influence persists to this day—was to give to the youth of the land the most practical and thorough collegiate pharmaceutical education at the lowest possible cost. The intent was not to build up a money-making institution, but to train men and women in pharmacy, and the original charter contained the provision (later eliminated) that the annual income of the College from all real and personal estate should not exceed five thousand dollars. And who shall say that there is not wisdom and truth in this Quaker philosophy of simplicity and thrift in education; because, it is *not* bricks and mortar that make an educational institution great—it is the brains within the bricks and mortar—the brains of earnest, able and devoted teachers reacting with the brains of youth, eager to learn, to think and to do!

During the first fifty years (1821-71) the instruction of the College was in materia medica, pharmacy and chemistry, and in the last four years of that period, in botany, also; and it was wholly didactic.

In 1846 an epoch-making advance was made, when pharmacy was recognized as a distinct branch by the establishment of the chair of theory and practice of pharmacy, and the chair of pharmaceutical and general chemistry was changed to chemistry. In 1867, the chair of materia medica was changed to materia medica and botany, and field work in botany was begun.

During the past fifty years (1871-1921) many additions to the curriculum have been made, such as analytical chemistry, practical or operative pharmacy, pharmaceutical chemistry, commercial pharmacy, pharmaceutical jurisprudence, chemical control in manufacturing pharmacy, scientific research, bacteriology and hygiene, Latin and pharmaceutical arithmetic, as well as special courses in technical chemistry, applied bacteriology, technical microscopy, physiologic assaying, clinical chemistry, advanced pharmacognosy, and perfumery, and the post-graduate courses leading to the degrees of bachelor of science in pharmacy, chemistry, pharmacognosy and bacteriology.

In 1897, the chair of materia medica and botany was divided into materia medica, including physiology, and into botany, including pharmacognosy.

In 1868, when the College moved to its present site, it had three instructors; today it has twenty-three, then 146 students, to-

day more than 600; then, no women students, today fifty; then, no laboratories, today six; then, no post-graduate courses, now four leading to degrees.

In 1920, in order to expand its courses of instruction, the charter was amended and the title changed to the Philadelphia College of Pharmacy and Science.

It is impossible at this time to more than briefly mention the teachers of the past, but during the first twenty-five years those who deserve especial mention are Samuel Jackson, George B. Wood, Joseph Carson and Franklin Bache, all of whom exercised potential influence during this formative period of American Pharmacy.

During the next fifty years the list embraced such widely known authorities in pharmacy as Robert Bridges (1842-79) whose lovable character and long years of unselfish devotion to the College has enshrined him in the hearts of all; Edward Parrish (1864-72), an exceedingly able and inspirational teacher, and the author of the first distinctively American textbook on the practice of pharmacy; John Michael Maisch (1866-93), whose constructive work for the upbuilding of pharmaceutical botany, materia medica and plant-chemistry will last as long as the name of pharmacy endures; and William Procter, Jr. (1846-66, 1872-74), whose researches in pharmacy gave a wonderful impetus to the growth and development of American pharmacy, made it known the world over, and won for himself the name of "The Father of American Pharmacy."

And William Procter, Jr., was succeeded by one who lived in our own time—"the noblest Roman of them all," one who as pharmacist, teacher, educator, author and executive—especially as the Chairman of the Committee on Revision of the U. S. Pharmacopœia for two successive decades—was the outstanding figure of American pharmacy in his day, the teacher of teachers, and the genial warm-hearted, inspiring friend of us all—Joseph Price Remington (1874-1918). "And we ne'er shall look upon his like again."

And then there was one who stood next to Remington, who was most largely instrumental in making the course of commercial training of the College (established in 1899), the first of its kind in the country, so successful, who became one of the foremost figures in American industrial pharmacy, and who loved his Alma Mater and never forgot her, even unto death—Frank Gibbs Ryan.

Motives of delicacy preclude my saying much of those who are

still living, honored representatives who have done yeoman service in the upbuilding of our institution, but the present sketch would be most incomplete did I not refer to one who has borne the heat and burden of the day for the past forty-three years as a teacher in our institution, one who has won national and international renown as a master-mind in pharmaceutical and industrial chemistry—our own, our honored, and our loved Samuel Philip Sadtler.

Quizzing was early instituted at the College and was conducted first by the professors themselves, and in the last 70's, by quiz-masters approved by the Committee on Instruction. In 1880, quizzes were authorized by the Alumni Association, and this constitutes the cornerstone of the present system of quizzing reviews. Later (1886) these were combined with the College reviews and made compulsory (1895), the College assuming full charge.

In 1821, the conditions of the practice of pharmacy were primitive. As Edward Parrish (AMERICAN JOURNAL OF PHARMACY, 1871, 481) stated, in 1871, in an introductory lecture to the fiftieth course of the Philadelphia College of Pharmacy:

"Fifty years ago when the College was established, almost every considerable drug store had something like a laboratory attached, where some of the few chemicals then in use and all the galenical preparations were made, and where nearly all the crude drugs were assorted, garbled and packed. The apprentices then enjoyed a wholesome development of muscle through wielding the ponderous pestle, handling the sieves and working the screw-press. He learned how to make pills by the wholesale, to prepare great jars of extracts and cerates, to bottle castor oil, Turlington's Balsam and opodeldoc by the gross, and what he lacked in the number and variety of articles he dealt in, was made up by a greater extent of his operations and the completeness with which, in a single establishment, all the then-known processes were practiced. Very many physicians then dispensed their own prescriptions, drawing the supplies from the druggists, but gradually the separate prescription counter was added to the drug stores, and the dispensing stores, as we now call them, became numerous, and the wholesale druggists gradually ceased to supply the public directly."

Our Quaker forbears realized that pharmacy was both an art and a science, and to be a master of the craft the pharmaceutical student must have practical instruction as well as theoretical, and from the first they required that the candidate for graduation from the College shall have a "practical experience of at least four years

with a person or persons engaged in and qualified to conduct the drug business." Thus vocational training was first established in pharmacy as a prerequisite for graduation.

About the time of the Civil War, a radical change took place in the retail drug business. The manufacturing of drugs and chemicals was taken over by manufacturing houses, more and more, the old apprenticeship custom of legally indenturing youths to learn "the drug and apothecary business" rapidly fell into disuse and the character of practical experience in the retail drug store changed, becoming less and less adequate, so far as manufacturing was concerned; although the underlying principle of drug store experience, with its familiarity with work-a-day technique, continued fundamentally sound. Hence, it became evident, that the College should give laboratory instruction; but the means of the College were limited, and it could not see its way clear, at this time, to give such instruction, especially as it was contemplating the erection of new buildings in the near future.

Next to its teachers, the biggest asset of a College is its alumni, directly and indirectly—directly in exemplifying its teaching and indirectly by its work for the Alma Mater; and no college in any land has more earnest, loyal and enthusiastic alumni than has the Philadelphia College of Pharmacy, including those of the Medico Chirurgical College merged with our College in 1916, and who, in season and out of season, are voicing their praises of its work and worth; and that their words are not idle words, is shown by the fact that probably 85 per cent. of the matriculants of the College come through the influence of its alumni.

As Richard M. Shoemaker, fifty-nine years a graduate of this College and the first treasurer of the Alumni Association (1864), and beloved by all, writes me: "The Alumni Association of the College always has been and is the backbone of all the energies for the advancement of the institution."

And we cannot mention the Alumni Association without mentioning Edward C. Jones, '64, who with his classmate, Albert E. Ebert, '64, founded the Alumni Association, and worked indefatigably for the College and its students. The vessel of clay that held his soul may have failed perhaps to reflect its beauty, but his personality had a charm that endeared him to all; and the good he did lives after him.

And then there was Thomas S. Wiegand (1825-1909) typical of the old school Philadelphia druggist of the last century, who sought by precept and practice to establish pharmacy in this country on a scientific and professional basis; he was elected President of the Alumni Association in 1865, and re-elected for six consecutive terms, and was Actuary of the College for twenty-two years (1887-1909), and as the "Students' Friend" was ever "their very present help in time of trouble." Many of the alumni will recall how much they owe to the wise counsel of that dear spirit of college days whom they lovingly and with all respect called "Uncle Tommy."

In 1864, the Alumni Association began a movement for the raising of funds for the equipment of a chemical and pharmaceutical laboratory; by 1867 the subscriptions had amounted to nearly $5000, and in 1870 it established a laboratory for instruction in practical chemistry and pharmacy in charge of Prof. John M. Maisch, the first of its kind in America. In 1872 the laboratory was turned over to the College by the Alumni Association. In 1876 its two divisions of work were partially segregated, Prof. Remington giving a course in pharmaceutical manipulations, and in 1878 he assumed full charge of the pharmaceutical laboratory (or laboratory of operative pharmacy), while Prof. Maisch confined his instruction to the chemical laboratory. In 1903 an optional course in dispensing was inaugurated, and the following year it became a part of the regular course.

In the chemical laboratory, Prof. Maisch was succeeded as director by Frederick Belding Power (1881-83), whose famous research work, later, in phytochemistry in the Wellcome Research Laboratory of London is known to you all, and he by Henry Trimble (1883-98), whose research work on the tannins is classic.

The microscopical laboratory was originated also by the Alumni Association, commencing with 1882-83, the Association controlling the instruction in this department until 1894, when the College assumed charge of it as the botanical and microscopical laboratory.

In 1899 optional laboratory courses were established in bacteriology, the study of powdered foods and drugs, fungi and fungous diseases, morphology and physiology, and systematic botany, and in 1913 bacteriological laboratory work became a part of the regular course.

With the enactment of the Federal Food and Drugs Act of

1906, it became apparent that skilled food and drug technicians would be necessary to ensure the proper enforcement of the law, and in 1907 the College secured, largely through the personal solicitations of the late Mahlon N. Kline and Joseph P. Remington, contributions of some thousands of dollars with which it was enabled to erect a food and drug laboratory building and inaugurate a course in food and drug analysis.

Equal in importance to pharmaceutical education is pharmaceutical research, because pharmaceutical practice is, in effect, applied education, and education is applied research; and upon the bases of research, education and practice rest the science and art of pharmacy.

Our Quaker forbears recognized the vital importance of systematized research and in 1821-29 published irregularly a journal devoted to research under the name of the *Journal of the Philadelphia College of Pharmacy*. Beginning with April, 1829, the Journal was issued at regular stated periods, and in April, 1835, the title was changed to the AMERICAN JOURNAL OF PHARMACY. It is not only the earliest periodical of its kind in the world, but it is recognized, at home and abroad, as the leading scientific pharmaceutical periodical of this country.

During the past century, the JOURNAL has published 50,000 reading pages, the larger part of which has been research work in pharmacy, chemistry, pharmacognosy and science, (Note, please, the significance of the initials of these—P. C. P. and S.!) by the faculty and members and contributors to the JOURNAL. Thus, John Farr, of Farr and Kunzi (later Powers and Weightman), in a paper read before the Philadelphia College of Pharmacy, of which he was a member, at a meeting held December 27, 1825, on the subject of "Extract of Quinine" (Proceedings of the Philadelphia College of Pharmacy—later the AMERICAN JOURNAL OF PHARMACY, Vol. 1, No. 2, 43), made the following statement: "In the summer and autumn of 1823, a season peculiarly memorable to Philadelphians by reason of the alarming prevalence of intermittent and other fevers, sulphate of quinine was first successfully prepared here," three years after its discovery by Pelletier and Coventou; and it should be stated, also, that Zeitler and Rosengarten (predecessors of Rosengarten and Sons), likewise made quinine sulphate in 1823, their first sale being in December of that year. And it may be added, that "morphine

sulphate and morphine acetate were first manufactured (in this country) by George D. Rosengarten in 1832; and the mercurials and strychnine sulphate in 1834" (Rosengarten and Sons, by William McIntyre, AMERICAN JOURNAL OF PHARMACY, 1904, 303). All of which activities were doubtless inspired by the spirit of original research developed by the College. And William Procter's discovery of the properties of the salicylates (1842) led to the manufacture of synthetic oil of wintergreen and the salicylates. Thomas J. Husband first developed (1837) the manufacture of heavy magnesia in this country. Robert Shoemaker first made (1848) glycerin commercially. Charles Shivers first developed the manufacture of adhesive plaster, making enormous quantities for the Government during the Civil War. William R. Warner first made (1857) sugar-coated pills. Alfred Mellor and Henry N. Rittenhouse first developed the manufacture of licorice extract. And C. Lewis Diehl and William Procter, Jr., first made the process of percolation commercially practicable.

The most important discovery of the Twentieth Century—as important as that of morphine, strychnine and quinine one hundred years ago—was that of diphtheria antitoxin by Behring in collaboration with Kitasato and Wernicke in 1890 and 1892. This discovery reduced the mortality of diphtheria from 40 per cent. to less than 10 per cent. and saved millions of lives. Tetanus antitoxin was discovered by Behring and Kitasato in 1892. During the World War its value as a life-saver was amply demonstrated. Ten per cent. of the wounded on the battlefields of France were attacked by the tetanus bacillus and 90 per cent. of these died of lockjaw. The call came for tetanus antitoxin and millions of doses were supplied to the armies of the Allies, resulting in the control of the deadly infection. These discoveries were speedily followed by others of equal value as life-savers. Typhoid fever, which hitherto had killed more soldiers than the bullets of the enemy was banished from the armies by anti-typhoid vaccination.

It is a matter of pride to us that these wonderful discoveries have largely been made available by our fellow alumni-graduates of the Philadelphia College of Pharmacy, as the H. K. Mulford Company, the earliest and largest producers of biologic products in this country, and who so promptly and successfully met, by means of an immense reserve stock, the call of the allied armies for such products during the World War.

And in the laboratories of the College many workers have solved many problems that have found important industrial applications, while from the faculty and alumni have come original papers of great practical value to medical and pharmaceutical science.

In this work the library of the College with its 20,000 volumes constituting the largest and most valuable pharmaceutical library in the United States, has been found to be of incalculable service; and next in importance has been its museum and herbarium with its many thousands of medicinal plants, its rare and typical exhibits of crude drugs, its raw materials, and its manufactured drugs from all parts of the world.

In the literature of pharmacy and allied science, the College has always been most actively represented, its faculty having issued nearly 200 volumes. Thus, the *U. S. Dispensatory* was founded in 1833 by George B. Wood and Franklin Bache, both of the faculty; John M. Maisch (with Alfred Stille, M. D.) founded the *National Standard Dispensatory* in 1879; Robert Bridges was the American editor of Fownes' *Chemistry* (1845-78), and of Graham's *Elements of Chemistry* (1852); William Procter, Jr., was the American editor of Mohr and Redwood's *Pharmacy* (1849); Edward Parrish wrote his first *Pharmacy* in 1855; Joseph P. Remington's textbook on *Pharmacy* has been the standard textbook on pharmacy since 1885, in this country and many foreign lands; John M. Maisch published in 1881 the first textbook on *Materia Medica* in this country; Henry Kraemer wrote his first *Applied and Economic Botany* and *Pharmacognosy* while at the College (1897-1917); Henry Trimble published his *Tannins;* Frank X. Moerk issued his *Qualitative Chemical Analysis;* Samuel P. Sadtler (with Virgil Coblentz) published his *Pharmaceutical and Medical Chemistry,* and his own *Industrial Chemistry;* Heber W. Youngken issued his *Pharmaceutical Botany* and *Pharmacognosy;* John A. Roddy issued his *Medical Bacteriology,* and Paul S. Pittenger published his *Biochemic Drug Assay Methods;* and with these should be included Julius W. Sturmer's admirable *Pharmaceutical Latin* and *Pharmaceutical Arithmetic,* as he has been affiliated with the College since the Chi-merger of 1916. And there were many formularies and other textbooks published that are not now in general use.

Prior to the U. S. Pharmacopœial Convention of 1850, pharmacists had no active part in the revision of the U. S. Pharmacopœia,

the work being done by medical men. But at the 1840 Convention the Philadelphia College of Pharmacy presented for consideration "a complete revised copy of the Pharmacopœia elaborated with ability and great industry, and the Committee accepted after deliberate examination, nearly all the suggestions" (U. S. P. IX, X); and thus was paved the way, logically, for the representation of pharmacists in all subsequent revisions, and in all of these the College has been most ably represented. Twelve of the thirty-three present pharmaceutical members of the Committee of Revision are P. C. P. men, and the last three Revision Committee chairman—Remington, LaWall and Cook—have been (or are) members of the faculty of the College.

The American Pharmaceutical Association, which stands for the highest ideals of pharmaceutical practice, and is the backbone of professional pharmacy in this country, was organized in the Philadelphia College of Pharmacy in 1852, its first president being Daniel B. Smith, the then president of the College; and from the time of its organization, the members and graduates of the College have been so active in its work, occupying many important official positions, and in the various State and local pharmaceutical associations, in the State Boards of Pharmacy, and as teachers in many schools of pharmacy, that the College has often been referred to as the "The Mother School of American Pharmacy."

What of the future? The past is yesterday and the future is tomorrow! We have been given a glorious heritage and must maintain the traditions of the fathers and justify their faith in us. How can this best be done? It seems to me that five things, chiefly, are essential: (1) Better education, (2) better legislation, (3) better practice, (4) better relations with the medical profession, and (5) better research work.

We must have better education, that is, higher entrance requirements, better facilities for instruction, including a drug plant garden, and better courses of instruction. Beginning with 1923-24, the College will require high school graduation, or it's equivalent, for entrance, and we are now working for better facilities and advanced instruction.

And it may be possible for the College to give a pre-medical course for medical students provided such course is organized on a scholastic basis and approved by the Association of American

Medical Colleges. The number of medical students in the United States is rapidly increasing and it would seem that the College could readily teach pre-medical students physics, biology (embracing bacteriology), biological chemistry, and pharmacology, together with medical pharmacy, medical chemistry and medical pharmacognosy, and probably mathematics and languages. Such a course would form an ideal premedical course.

We must have better legislation, especially prerequisite legislation, and this need is vital, not only for the good of American pharmacy, but for the better service of the American people. Today, less than one-half of the forty-eight States of the Union have prerequisite laws, and the public will not be properly served until every State of the Union has such a law; and we must have universal reciprocity between State Boards of Pharmacy, or national licensure; and we must have simpler and more efficient pharmacy laws by State and nation.

We must have better practice along professional or technical lines that will be of direct value to the medical profession in the diagnosis and treatment of disease; there must be a sharper differentiation by the pharmacist, in his daily work, between legitimate commercial pharmacy and illegitimate, or real pharmacy will cease to be; and it may be that we will have in this country, in the future—two kinds of stores—pharmacies and drug stores, the former for professional service and legitimate commercialism, and the latter crassly commercial.

We must have better relations with the medical profession by deserving it—by perfecting our individual abilities and directing our work primarily along professional and scientific lines that will appeal to the medical profession and win their sympathetic support. In the past we have not had this. Let us hope that under the inspiring leadership of our new President, William Clarence Braisted, the medical profession will come to realize the potential possibilities of pharmacy, acting in co-operation with medicine as a sister art.

Pharmacy is the study of the reaction of drugs without the human body, and therapeutics is the study of the reaction of drugs within the body, and the one cannot properly function without the other. In a word, pharmacy is the physico-chemistry of drugs, and therapeutics is the biochemistry; and practically pharmacy is as vital to medicine as therapeutics or any other medical art.

We must have better research work, because research is the life-blood of education and practice. As Dean Charles H. LaWall writes me, "The future development of pharmacy is largely dependant upon the stimulation of research, especially its inculcation in the student-body. The work of the College in the past has been of the highest character, but it has been done unsystematically, and was largely a matter of chance that it was done at all. Men like Maisch, Procter, Remington, Sadtler, Kraemer and others have simply bubbled-over with initiative, and their efforts have enriched pharmacy and made it better. Today, however, the output is limited, because every member of the faculty is driven full-speed in taking care of his teaching and accessory work. To overcome such a handicap, the teachers should have more assistants for instructional work. The progress of any department of the College could then be measured not only by its instructional results, but also by the quality and quantity of original work it turns out, and the College would have a standing among other scientific schools that instruction alone could not give. Furthermore, students, graduates, members of the College, and others, would be inspired to follow the example of the faculty, and the field of research would be developed and coordinated." And as if in anticipation of such a possibility, the Board of Trustees of the College has recently established a sub-committee on research of its Committee on Education to systematically promote research work in pharmacy and correlated science.

And the field of research is practically unlimited. As John Uri Lloyd, a Master in Pharmacy of this College (1897), and one whose research work in pharmacy for the past fifty years stands out like a beacon-light at home and abroad, writes me: "In my opinion, the field of research is as yet scarcely invaded. Whoever enters it should, with each subject, as a foundation, have his feet on the work others have accomplished, then with open mind, raise his eyes to the blue sky above. He should start with a hypothesis gained from study or experience with related products, and yet expect to fail in whatever thought had speculatively advanced. Disappointment brings then no pain. He should be so bold as to question orthodox theoretical rules and formulæ, and in the face of 'authority' create images and plans of procedure of his own. And yet he should be so timid as to shrink from personal criticism of others, realizing that his own self will rise before him as perhaps the one most subject to criticism un-

der the backward glance. If concerned in the exactions of science, he should expect resistance from those whose idols he touches with even the kindliest intent. If conscious of the correctness of his views he should make no retort; *time* will care for *fact.* If he has indiscretely voiced false theories based on fallacious judgment, he should thank the man of the present for service rendered in his disillusionment, resting assured that *time* would later have served the same purpose. If given a moderate period of life the backward glance will surely show a pathway littered with his own broken vases, shattered into fragments by himself. The great charm of research may be defined as the construction of new edifices out of those demolished, and in plant research, the defining and describing of natural textures and plant structures. In this the doors to be opened by the systematically trained scientists of the near future will surely make the life-wanderings of empiricists, with whom this writer is to be classed, pioneer offerings serviceable perhaps mainly as an inspiration to those to follow."

What will the next one hundred years bring our Alma Mater? No man knoweth; time only can tell. And yet paraphrasing Longfellow, let us make our Alma Mater our Ship of State, so strong and great and cry to her: "Sail on! Our hearts, our hopes, our prayers, our tears; our faith triumphant o'er our fears, are all with thee—are all with thee!"

SALICIN CONTENT OF BRITISH COLUMBIAN WILLOWS AND POPLARS.

By R. H. Clark and K. B. Gillie.

These determinations on the salicin content of various species of willow and poplar native to the Province of British Columbia are the first of a series of investigations on the possibility of economically cultivating within the Province several species of both native and introduced essential-oil and drug-yielding plants.

For many years the Provincial Botanist, Professor John Davidson, has had numerous inquiries, from wholesale drug manufacturers and others, asking advice on the cultivation and collection of medicinal plants. To secure the necessary information experiments are being carried out on a number of well-known drug plants with

a view to ascertaining the relation between the soil and climate of the Province and the percentage of drug produced by the plant, and also to experiment on the effect of various fertilizers in relation to the size of the crop and percentage of drug. Among the subjects to be investigated in the near future are: Cascara sagrada from Rhamnus Purshiana, atropine from Atropa Belladonna, stramonium from Datura Stramonium, aconite from Aconitum napellus, digitalis from Digitalis purpurea, oil of spearmint, oil of peppermint and oil of Monarda Fistulosa. These investigations will be carried on jointly by the Departments of Botany and Chemistry.

There are several reasons why such an industry might thrive within the Province; we have a large number of plants indigenous to the Province which are known to yield oils and other drugs of economic value; we have climates and soils of so varied a nature that it is possible to find localities suited to the cultivation of such plants; there is a large demand for soap, pomades and similar perfumed products in the Oriental markets, easily accessible from the western coast. There is no doubt that many of the plants adapted to a temperate climate could be grown somewhere within the Province. The chief questions arise in connection with a precise choice of locality and the cost of production, and this again would depend on the cost of cultivation and also on the quality and quantity of the drugs which could be obtained. Such questions can only be answered by experiment.

SALICIN.

Salicin [ortho-hydroxy-benzyl-glucoside, $C_6H_4(OC_6H_{11}O_5)$-$CH_2(OH)$], was one of the first natural glucosides to be discovered. It occurs in most, but not all, species of willow and poplar bark. It is hydrolysed by mineral acids and by emulsin of almonds, to dextrose and o-hydroxy-benzyl alcohol. As determined by this enzyme action, salicin must be a glucoside.[1] Populin, another glucoside, also occurs in the leaves and bark of poplars. It is not, however, hydrolysed by emulsin of almonds.[2] On the other hand, it may be hydrolysed by barium hydrate to benzoic acid and salicin. Salinigrin, a third glucoside, has been found in only one species of willow, Salix discolor.[3] Helicin, a glucoside isomeric with salicin does not occur naturally.

[1] Fischer, Zeit. Physiol. Chem., 26, 61, 1898.

[2] Allen's Comm. Organic Analysis, vol. 7, p. 100.

[3] Jowett & Potter, Trans. Chem. Soc., 77, 707, 1900.

The bark from the following species, Salix Nuttallii, Salix Hookeriana, Salix sitchensis, Salix lasiandra, Salix purpurea, Populus trichocarpa and Populus tremuloides, were analysed. We wish to thank Professor John Davidson for his kindness in providing the various samples.

METHOD OF ANALYSIS.

The bark was dried for forty-eight hours at a temperature of about 110 degrees. Two samples of each, weighing twenty grams, were taken, and digested separately for three hours with boiling water and the solution filtered. Two grams of lead acetate were then added to the filtrate to precipitate the proteins, which were removed by filtration. The excess of lead was then precipitated by the addition of the required amount of sulphuric acid, and the liquid filtered. To this filtrate was added 100 cc. of the emulsin of almonds solution and the mixture allowed to stand sixty hours, at which time the solution was diluted to two litres and two portions of 100 cc. were taken for analysis with Fehling's solution. The weight of glucose present being found by reference to Munson and Walker's tables.[4] One mole of salicin gives on hydrolysis one mole of glucose.

The emulsin of almonds solution[5] was prepared from sweet almonds, from which the oil had been pressed, as follows: The press cake was macerated for twenty-four hours with water, to which a small amount of chloroform was added. The mixture was then strained through a cloth and two drops of acetic acid were added per 100 cc. of the liquid for the precipitation and removal of the proteins. To the filtrate was then added an equal volume of alcohol, 50 cc. at a time, which caused the enzyme to come down as a fine precipitate, which was filtered off, washed with alcohol and immediately re-dissolved in water, to which a small amount of toluene had been added. The solution of emulsin of almonds so obtained was tested by treating solutions containing known amounts of pure salicin. It was found that the hydrolysis was complete after sixty hours. The results obtained were correct to within less than 1 per cent.

As is seen from the following table of determinations the duplicate analyses are in close agreement, whilst the salicin content of the various species of willow and poplar show a considerable variation.

[4] "Food Inspection and Analysis," Leach.

[5] Allen's Comm. Organic Analysis, vol. 8, p. 6.

Likewise the spring samples in most cases run higher than the corresponding fall samples, in the cases of Salix Hookeriana and Salix sitchensis a most notable difference was found.

TABLE OF ANALYSES.

	FALL SAMPLES.			SPRING SAMPLES.		
Species	*(1)*	*(2)*	*Av'g.*	*(1)*	*(2)*	*Av'g.*
Salix Nuttallii	3.88%	3.92%	3.90%			
				4.47%	4.51%	4.49%
Salix Hookeriana	0.79	0.84	0.81	5.18	5.00	5.09
Salix sitchensis	2.68	2.92	2.80	7.32	7.43	7.38
Salix lasiandra	2.45	2.55	2.50	2.50	2.53	2.51
Salix purpurea*	....	....	....	3.78	3.88	3.83
Populus trichocarpa	0.95	0.96	0.955	3.83	3.89	3.86
Populus tremuloides	3.80	3.74	3.77	2.42	2.48	2.45

It might be pointed out that there is a large quantity of bark at present annually available at the Vancouver basket factory. In addition there is a very large supply of native willow on the lower mainland of the Province and on Vancouver Island.

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THE ORGANO-METALLIC BODIES.

By HENRY LEFFMANN, M. D.

Of the many classes of organic compounds those in which metallic elements are joined directly to nitrogen or carbon are probably the furthest removed from the what was in earlier days considered specific features of organic substances. Being all synthetic products, they have been very largely studied as matters of pure science, but of late years a practical interest has attached to some of them, and research has received an additional spur.

The first production of an organo-metallic compound seems to have been due to a (probably random) experiment in 1760, when Louis Claude Cadet de Gassicourt, a military apothecary in Paris, distilled a mixture of arsenous oxide and potassium acetate, and

*Cultivated variety imported from Japan and planted on LuLu Island for basket-making trade.

obtained a liquid fuming in the air and capable of spontaneous combustion. The nature of this long remained unknown, and it was merely designated as *"Cadet's Fuming Liquor."* A radicle termed "kakodyl" As $(CH_3)_2$, is the basis of the principal ingredients in the mixture, and in 1842 Bunsen by a series of most interesting and wonderful researches, elucidated the chemistry of the subject and showed that the kakodyl radicle can form a large number of compounds, most of which are highly poisonous. One striking exception to this quality was noted in the case of kakodylic acid, $HAs(CH_3)_2O_2$, the toxicity of which was found to be much less than the content of As would indicate. The investigation of such compounds involves much risk, and Bunsen lost an eye in consequence of the explosion of a tube in which he was distilling one of the compounds. Kakodylic acid was introduced in medical use, but has not found any important applications, and all these arsenicals have given way to the benzene derivatives of which arsphenamin is the best known.

The question of susceptibility to ionization is one which must be taken into account in judging of the physiologic effect of any substance, and in the case of poisonous metal, the position of it in the ion will also determine largely its effects. The contrast between the cyanides and the ferrocyanides exemplifies this fact.

The chemistry of the organic compounds of arsenic and antimony has been extensively treated by Gilbert T. Morgan in a work issued a few years ago and a glance at this will show the extent of the researches along this line and the variety and complexity of the compounds already known. It is well known that the original name of arsphenamin, "606," was provisionally given because it was the 606th. derivative that was prepared in the effort to find an arsenical that should have a much higher germicidal action than general toxicity, so as to permit it to be used in rather large doses in the annihilation of the specific germ of syphilis. The investigations along this line have continued and today derivatives analogous to arsphenamin have been produced in great number, among which are some that appear to be better adapted to therapeutic use than the original compound.

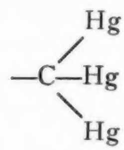
The analogy between arsenic, antimony, nitrogen and phosphorus renders it possible to obtain from the former two compounds of the same type as ammonia and phosphin. These, as might be

expected, show high poisonous properties, and have had no important applications except as asphyxiating gases in war.

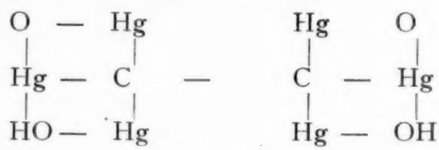
Mercury yields a large number of organo-metallic compounds. The literature of this phase of the subject is extensive, but until recently has not been collected in convenient form, as has been that relating to arsenic and antimony. The enterprise of the American Chemical Society has made available a comprehensive collection of the data concerning organo-mercury compounds, in a volume prepared by Dr. F. C. Whitmore of the Northwestern University, just published. As in the case of the arsenic compounds, the history begins with a somewhat random experiment. In 1843, A. W. Hofmann distilled a mixture of aniline and mercuric chloride and obtained a compound containing mercury in union with a hydrocarbon group, but apparently the exact structural formula of this has not yet been ascertained. In 1850, Frankland noted that metallic mercury acts on ethyl iodide, later found that methyl iodide is changed by the same metal into a methyl mercury iodide, CH_3HgI, and that a similar compound can be obtained from the ethyl radicle. A tragic incident occurred in connection with the early work on these substances, for two of the assistants, Dr. Ulrich and Dr. Sloper, who were working in the laboratory of St. Bartholomew's Hospital, London, where the research was being carried out, were fatally poisoned. Another London chemist accused Dr. Frankland of sacrificing his assistants by imposing on them this dangerous work instead of doing it himself, and for several months the columns of the *Chemical News* were hot with the exchange of correspondence. It appears, however, that no blame can attach to the chief. The methyl and ethyl compounds are liquids of high density, strongly refracting and dispersive, and it was thought that they might be available for filling hollow prisms, but their high poisonous qualities constitute a serious interference.

Interest in the study of organic mercury compounds has been much increased for the same reason that the arsenic compounds have acquired prominence, the use of mercury in syphilis. The need has especially been for non-ionizing compounds which may be used in association with the arsenicals. Just about the time that Frankland obtained the above-mentioned compounds, Sobrero and Selmi discovered another type. By heating mercuric chloride and potassium hydroxide in alcoholic solution, they obtained a yellow slightly ex-

plosive substance containing mercury and carbon, but many others attempted without success to confirm their result. Later, K. A. Hofmann obtained a series termed the "mercarbides" containing the



Some notion of the complexity possible in these substances is shown in the formula of ethane hexamercarbide



A different arrangement results when sodium amalgam is used with the organic bromide and iodides. Both bonds of the diad mercury are attached to the carbon. These reactions, however, so far have been obtained only in the presence of an ester such as methyl or ethyl acetate, which acts as a catalyst, inasmuch as it can be recovered unchanged at the end of the reaction.

Out of the immense mass of compounds of these types a limited number—about two score—are already in the market under copyrighted titles and recommended for medicinal purposes. Some of them contain both mercury and arsenic. How many of them will stand the test of scientific experience it is impossible to say, but all therapeutic history goes to show that ingenious advertising is often the main cause of the popularity of a synthetic drug. However, the scientific features of the organo-metallic compounds will always have a fascination for the chemist.

MUIRA-PUAMA.*

BY HEBER W. YOUNGKEN, Ph.D.

This drug, concerning which comparatively little has been written, has been employed in Brazil and France in the form of fluidextract and other preparations for the treatment of various nervous disorders. In recent years it has been shipped from Para and Rio de Janeiro, Brazil, to manufacturing pharmaceutical houses in the United States, where it is made into a fluidextract, which is then sent back to Brazil, there being no particular demand for it here.

The writer, being interested in the botanical source and anatomy of this new article, procured a good-sized sample from one of Philadelphia's manufacturing pharmaceutical houses. This was compared both as to physical and microscopical features with two samples of a root also labeled "Muira-puama," in the crude drug collections of the Philadelphia College of Pharmacy and Science. The three specimens revealed a similar structure and so were undoubtedly of the same botanical source. On the label of one of the specimen jars containing the root appeared the botanical origin, "*Liriosma ovata* Miers."

DESCRIPTION OF PLANT.

Lirosma ovata Miers[1] is a small tree indigenous to Brazil and belongs to the Olive family. Its leaves are short, petiolate, glabrous, up to three inches long and two inches broad, broadly ovate, attenuated at the summit, slightly reflexed along the margin; upper surface light green, lower surface dark brown; venation pinnate-reticulate, more conspicuous on the upper than the lower surface; midrib pubescent above, smooth below. Its inflorescences consist of short axillary racemes, each of four to six flowers.

DESCRIPTION OF ROOT.

Conical, nearly straight, tapering to a small point, from one-half to one and one-half feet in length and from one-eighth to one and one-half inches in diameter; externally light-brown to grayish-brown, faintly longitudinally striated and beset with short sharp projections, which occasionally unite two or more roots; fracture strongly tough and fibrous; internally light-brown exhibiting a thin bark and broad wood; odor faint; taste slightly saline and acrid.

*Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Philadelphia Pa., June 10, 1921.

HISTOLOGY OF ROOT.

Sections of the root disclose the following microscopical characteristics, passing from periphery toward the centre:

1. Cork, composed of several layers of tabular cells with brownish contents and more or less lignified walls.

2. Phellogen, of clear meristematic cells.

3. Secondary Cortex, composed of a number of layers of parenchyma, some of the cells of which contain a reddish-brown resin, others starch, still others monoclinic prisms of calcium oxalate. Imbedded in this region are scattered islands of sclerenchyma, accompanied by crystal fibers, the individual cells of which contain rhombohedral crystals of calcium oxalate.

4. Phloem, a narrow zone of sieve tubes and phloem parenchyma. Isolated groups of thick walled bast fibers accompanied by crystal fibers are found amongst the other phloem elements.

5. Cambium, a prominent zone of meristematic cells.

6. Xylem, a very broad central zone of radially arranged wood wedges separated by starch containing medullary-rays. Each xylem wedge is composed of numerous wood fibers with thick, lignified walls, scattered amongst which are starch and crystal containing wood parenchyma cells and tracheæ with bordered pores and simple pits. Crystal fibers containing monoclinic prisms of calcium oxalate frequently adhere to the wood fibers.

POWDERED DRUG.

Light brown; the characteristic elements being the following: Starch grains which are simple or 2-4-compound (usually 2-3-compound), the individual grains spheroidal, plano-convex, or bitruncate and up to 15 microns in diameter; numerous calcium oxalate crystals, both as crystal fibers and rhombohedra; numerous fragments of sclerenchyma fibers, the latter often accompanied by crystal fibers containing rhombohedral crystals of calcium oxalate; occasional stone cells with thick, lignified, porous walls; numerous fragments of tracheæ, some of which have bordered pores, others simple pits; resin cells with dense brownish contents.

PREPARATIONS.

In addition to the fluidextract, there are two preparations now used mainly by the French. One of these, "Pilula Potentin Composita" contains one grain of extract of muira-puama and one grain of ovolecithin to each pill. It is employed as a nerve stimulant and aphrodisiac in doses of 3 to 6 pills daily before meals.[2] The other preparation "Muiracithin" consists of the residue in vacuo of 100 grams of fluidextract of muira-puama and 5 grams of lecithin with a sufficient quantity of licorice powder added to make 100 pills. The dose given is three to four pills daily; one pill morning and noon and two in the evening.

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ABSTRACTED AND REPRINTED ARTICLES

EMPIRICAL FALLACIES (AND OTHERS).*

JOHN URI LLOYD, CINCINNATI, O.

Possibly it is proper for one who believes that to empiricism is largely due progress in life's advancement, as both serviceable in the beginning and supplying texts for subsequent research, to call attention to some of the fallacies of misapplied empiricism. A pleasure, is it not, to look back at the errors one held in the passing along of life, and a greater pleasure to utilize such errors for self-reflection and perhaps record them for the benefit of others.

A few yeas ago this writer, on a special research mission, was traveling through Asiastic Turkey. Observant was he of much that lay outside his direct field of study—many were the pleasurable in-

*From the *Eclectic Med. Jour.*, July, 1921.

cidents that recollection brings often now to mind, among others the story of "The Blessing of the Fig." With this legend in view, let us consider—

The Barren Fig Tree.—The writer observed that early in the springtime certain trees in the fig orchards of Turkey were seemingly far ahead of the great majority of fig trees. Also it was seen that these early fig trees frequented the edges of woodlands and in several instances hedged dividing fence lines as well as thickets along the sides of the road. On these trees the young figs were large before the fruit appeared on the laggards. The writer questioned why this early variety of figs was not more abundantly cultivated. Came the reply that these were barren fig trees and carried no figs to maturity. Came then the story, as follows:

These figs appear early, they grow to a certain size, and open from the rounded apex. From this orifice stream swarms of very small flies, which seek the fruit-bearing fig trees and inoculate them with the spores borne from the fig from out of which they came.

Said my informant: "The fig you have noticed is the wild fig. Its function seems primarily to bear a crop of insects. After these have escaped the fig withers, dies and drops to the ground. The tree bears no fruit; it is barren." In times remote, barren fig trees in an orchard were cut down as cumberers of the ground.

Mythology of the Barren Fig Tree.—Continued my informant: "In the early days, the priests, taking advantage of this insect fact not comprehended by the people, appointed each year, as a religious ceremony, a day for blessing the fig trees in the orchards. At that time, as has been stated, the barren fig tree was considered of no value, all being intentionally exterminated from the orchards. A festival day for 'blessing the fig' orchard was appointed for a day when the wild fig was ready to open and liberate the swarm of flies. The priest led the villagers to the wild figs, dressed in holiday attire and bearing branches culled therefrom laden with these figs the procession turned to the fig orchards. As the man of God blessed the fig trees the villagers threshed these trees with the boughs laden with the wild figs. This whipping of the trees of the orchard resulted in the liberation of flies throughout the entire orchard. These flies, seeking the young figs just appearing on the female trees of the orchard, fertilized them with the spores from the wild (barren) fig, and the orchard bore an abundance of figs.

Empirical Reasoning.—"What could be more conclusive than that this blessing of the fig orchards by the holy man, and the ceremony performed, resulted in the bountiful fig crop? Self-apparent it was, because fig orchards not thus blessed were comparatively barren.

"We know now," said my informant, "that the wild fig is the male, the fruit-bearing fig being the female, and that the spores that fertilized the fruit were carried from the male to the female fig by the insect that escaped from within the flower of the wild fig. Now, each orchard carries a number of wild fig trees. No longer is the blessing of the priest necessary."

Continued the educated Turk, my companion: "Some years ago came a demand from America for many thousand young Turkish fig trees. These were gathered and forwarded—but," said the Turk, "the Smyrna fig will not be profitably raised until America gets the Turkish insect that, escaping from the young flower of the barren fig tree, accomplishes the fertilization of the fig."

Apple Trees and Fish.—When the apple trees bloom in the springtime on the islands of Lake Erie, the bass bite best. The question comes at once to an observing empiricist, "What connection is there between the fish in the water and the flower on the tree?" He might rationally surmise that the influence of the fish makes the tree blossom, or that the blossoms of the tree bring the fish to the shoal. The man of science might perceive that the same warm sunshine that brings blossoms to the tree also entices the fish from the cold depths of the lake, to spawn in the warm water of the shallows.

Apple Tree and Morel.—Turn now your attention to the Kentucky apple orchard. Behold, when blooms the apple tree, the morel (an edible fungus) springs in abundance from about the base of the tree. Reasoning empirically, one might say that the bloom of the apple tree awakens the morel from out the earth. Another might perhaps reverse the thought, asserting that the morel's influence makes the apple tree bloom. Simple is this reasoning, but yet the question remains unanswered why the morel rises under the blossoming apple tree and not under the honey-locust but a short distance away.

Mystery of the Morel.—Take now this same morel. Go into the deep woodland about the time it appears in the apple orchard.

Search the woodland. No morel is likely to be found until the ash tree is reached, and here it may thickly stud the leaf mould. Within a radius of one hundred feet about an ash tree this writer has gathered a basket of morels, and in the entire woodland, excepting where grew an ash tree, has found no morel. The yellow poplar (*Liriodendron Tulipfera*) also sometimes serves to a lesser degree as a culturing shade host of the morel. Empirical reasoning would say that some influence of the ash tree favors the growth of the morel. Other reasoning might intimate that in times gone by the seed of the ash tree sprouted in a bed of morels, the progeny of which still lingers. The man of science says frankly, "I don't know," but with open mind he perhaps accepts that the root of the ash tree infects the soil with an unknown "something," be it bacteria or secretion, that favors the morel's growth.

Catalpa and Raspberry.—When blooms the catalpa tree by the wayside, the black raspberry ripens in the field and thicket. Observing this, the empiricist might say, "The blooming catalpa is the cause of the raspberry's ripening." Another may as rationally differ and argue that ripening raspberries bring the blossom to the catalpa. Judging by facts only, empiricism might thus neglect the heat and light cause that both ripens the raspberry and brings the bloom to the catalpa. The parellel might be extended indefinitely.

The Black Beech.—When start the leaves of the "Black Beech," red, even to crimson, dominates. As the season progresses the leaves darken and at last become black. Reasoning from observed facts, the empiricist might argue that a black coloring matter had been deposited in the leaf from which the red had faded. Comes the thoughtful investigation of the man of science. Lo, the black results from a combination of red and green chlorophyll, which in proper proportion makes the black pigment of the matured leaf of the beech. Passes further the scientific investigator, who shows that vegetable green is a mixture of blue and yellow. Did not very primitive people make shades of green by such admixtures? Thus yellow, blue and red makes black to pigment the leaf.

Clover Fertilizer.—These many years ago, observing farmers decided that red clover, raised on poor ground, then plowed under, enriched the earth even to fertilization sufficient for a subsequent

crop of wheat. "Imagination," said the chemist, for did not analysis show that clover was insufficient, or even nearly useless, in accepted food content? And yet the farmer was not convinced; he continued to raise clover to enrich his soil. Came then the man with the microscope. Behold, the roots of the clover swarmed with nitrogen-fixing bacteria. To this it might be added that beneath a black locust thicket blue grass luxuriates, and white beans thrive on poor, sandy soil, that mellilotus (sweet clover) asks no fertilizer when it covers Kentucky yellow clay dug from deep in the earth.

Sun Spots.—Comes to the sun a mighty "spot" that slowly passes across its face. Simultaneously a display of aurora borealis blankets our heavens. Electrical disturbances pervade the earth, telegraph wires refuse to "message," even lead fuses within brick buildings flash and burn out. What is more natural than to conclude that the earth-phenomenon is caused by the sun spot? But, might not another mind reason that suns and planets are but cells floating in space, and that both sun, earth and heavens respond in unison to an intercellular impulse in the ether that pervades all things?

Remedial agents there are, employed in confidence by observing physicians, though the man of science has not as yet fathomed the secret of their action. Helpless is he to account for phenomena known to his microscope, his biological efforts are fruitless, chemistry fails. The empiricist accepts these facts, he continues to employ the agents discredited by all but those who, by repeated experiences, have learned their uses. With the object of curing his patients, the observing physician walks the forbidden path of an ostracized "irregular."

But enough. None can forever suppress facts with theories, or by means of experiments that do not parallel or cannot fathom Nature's laboratory. The man of science shows why the blessing of the fig trees gave the crop of figs, why the apple blossoms when the bass spawn, why the raspberry fruit ripens when the catalpa blooms; but as yet he closes his eyes in despair and offers no scientific explanation as to why the morel makes its appearance under the apple tree in the orchard and the ash tree in the woodlands, and not in the same rich earth about the base of the beech, the hickory, the elm, the walnut or other trees in the forest shades adjacent to the ash. Such problems as these he will surely work out, and this writer

believes he will yet show how and why a single remedial agent, destitute of toxic qualities and mild to the taste and smell, as is the pith of the sassafras or the fruit of the hawthorn, may stimulate a life process that may change abnormal tissue, excite an exhausted muscle, soothe an inflamed and tender surface, or through some force encourage vitality to restore health.

IMPROVED DENIGÈS TEST FOR THE DETECTION AND DETERMINATION OF METHANOL IN THE PRESENCE OF ETHYL ALCOHOL.*, [1], [2]

By Robert M. Chapin.

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The examination of alcoholic products for methanol has been a problem of interest to many chemists. If a certain few published papers are consulted the matter would appear to be rather simple, at least from the qualitative side. But a thorough survey of the voluminous literature, comprising a large number of methods with contradictory comments and conclusions, does not lead one to undertake exacting work along this line with entire confidence.

One of the most recent investigators, Gettler,[3] having reviewed fifty-eight existing tests, recommends subjecting the sample to nine qualitative tests, sequentially applied. In passing it may be noted that his eighth test, a refractometric one, is essentially quantitative in nature, being based upon a numerical difference between physical constants, and is only secondarily of qualitative significance. Also his first seven tests are merely tests for formaldehyde, applied after treating the sample with a single oxidizing agent. If this oxidizing agent is capable of producng formaldehyde from any substance other than methanol, all the seven tests must be subject to a common source of error.

*From *Jour. of Ind. and Engr. Chem.*, June, 1921.

[1] Received February 16, 1921.

[2] Published by permission of the Secretary of Agriculture.

[3] *J. Biol. Chem.*, 42 (1920), 311.

Purely qualitative findings, however, seldom afford solid ground for action in matters of commercial or legal importance. The question "How much?" is almost certain to arise. It is a pertinent question here, inasmuch as several investigators[4] have stated that methanol is naturally produced in certain fermentations. If methanol, like fusel oil, is a normal constituent of alcoholic products, then the legitimacy of its presence in any case may be satisfactorily settled only by quantitative examination. The analytical chemist needs, first, a simple but dependable qualitative test which shall possess semi-quantitative value in that it is able to serve as a "limit test," and, second, a quantitative method which shall enable him to assert with positiveness very nearly the exact percentage present. The quantitative method must be subjected to intensive study in order:

(1) To develop its highest inherent precision.

(2) To devise methods for the elimination of interfering substances.

(3) In case elimination is impossible, to determine the size of the "blank" involved by the presence of each such substance.

The Denigès[5] test seems most promising for both qualitative and quantitative application. It consists in treating the alcoholic solution with potassium permanganate and acid, whereby methanol is oxidized to formaldehyde. The latter is detected by Schiff's reagent in the presence of sufficient sulfuric acid to prevent development of color from acetaldehyde. There appears no evidence that other proposed oxidizing agents, such as bichromate and acid or persulfates,[6] are inherently superior to permanganate and acid. The latter agent is pre-eminently simple and convenient, requiring no heat for its action and finally affording a colorless solution. No reagent effects a quantitative yield of formaldehyde. All require

[4] von Fellenberg, *Mitt. Lebensm. Hyg.*, 5 (1914), 172; *Biochem. Z.*, 85 (1918), 45; Takahashi, *J. Coll. Agr. Imp. Univ. Tokyo*, 5 (1915), 301; *J. Am. Chem. Soc.*, 39 (1917), 2721.

[5] *Compt. rend.*, 150 (1910), 832.

[6] Preliminary experiments have indicated that persulfates, especially in strongly acid solution, may produce a notable quantity of formaldehyde from pure ethyl alcohol. The possibility of such a reaction has been noted by previous observers in the application of several oxidizing agents. Bichromate and acid, in comparison with permanganate and acid, appears to afford a high yield of acetaldehyde from ethyl alcohol, but a low yield of formaldehyde from methanol.

strict adherence to a standard set of conditions under which it is assumed that a certain concentration of methanol originally present results in a certain concentration of formaldehyde at the end.

Likewise, for the demonstration of formaldehyde there appears to be no reagent any more convenient or reliable than Schiff's reagent, prepared according to the Elvove[7] formula. Its chief comparative disadvantage is the slowness of development of the final color.

QUANTITATIVE METHOD.

The Denigès' method has been used with more or less modification by a considerable number of investigators. Since in routine analyses following the procedure of Elvove the observed margin of precision seemed unnecessarily large, the whole process has been subjected to close scrutiny with a view to attaining greater precision. It was decided that 0.04 cc. of total alcohol should be the standard quantity for each test, which, including the necessary acid, should be made to a volume of 5 cc. The nature and proportion of the acid is of very great importance. The highest yield of formaldehyde results from slow action of permanganate in presence of low hydrion concentration; but practical considerations prohibit an inordinately long reaction time, while the total acid must be kept up to a safely high figure. The conditions finally chosen were the addition of 0.2 cc. of phosphoric acid (C. P., 85 per cent.), previously diluted to 1 cc. for accuracy in measurement, and an oxidation period of 30 min., instead of the 0.2 cc. of concentrated sulfuric acid and oxidation period of 3 min. employed by Elvove. Next, after deciding that the necessary permanganate should be added in a volume of 2 cc., it remained merely to find a concentration of the permanganate solution such that either more or less than 2 cc. of it would give a lower yield of formaldehyde than exactly 2 cc. The desired strength was found to be 3 per cent. In a similar way the volumes of sulfuric acid and Schiff-Elvove reagent were tested. Directions for the method may be given as follows:

[7] This JOURNAL, 9 (1917), 295. Fuchsin (0.2 g.) is dissolved in 120 cc. hot water. After cooling to room temperature there are added 2 g. of anhydrous sodium sulfite dissolved in 20 cc. water, followed by 2 cc. concentrated hydrochloric acid. The solution is diluted to 200 cc. and is allowed to stand 1 hour before use. If well stoppered in an amber bottle it may remain fit for use for several weeks. The Schiff-Elvove reagent appears decidedly superior to the original Schiff reagent, and should supersede the latter.

Dilute the solution, previously purified as necessary, to 1 per cent. by volume of total alcohol (Sample Solution A). Of this, pipet 10 cc. into a 50-cc. volumetric flask, add 10 cc. of a 4 volume-per cent. solution of pure ethyl alcohol, and make to the mark with water (Sample Solution B). Of the latter, likewise, dilute 10 cc. plus 10 cc. of the 4 per cent. ethyl alcohol to 50 cc. (Sample Solution C). Into 50-cc. tall-form Nessler tubes pipet 4 cc. of the three sample solutions. Prepare standard methanol tubes containing, respectively, 1, 2 and 3 cc. of a 0.04 volume-per cent. aqueous solution of pure methanol plus 1 cc. of 4 per cent. pure ethyl alcohol, plus sufficient water to make 4 cc. After the tubes are properly arranged in a rack the following operations are put through in strict parallelism remembering that each reagent is to be added to all tubes before any are mixed:

1—Add 1 cc. of a 1 in 5 volume solution of phosphoric acid (C. P., 85 per cent.), and mix.

2—Add 2 cc. of 3 per cent. potassium permanganate solution, mix, and let stand 30 min.

3—Add 1 cc. of 10 per cent. oxalic acid solution, mix, and let stand till a clear brown (about 2 min.).

4—Add 1 cc. concentrated H_2SO_4 (C. P.), mix, and let stand a few minutes for temperatures to become equal.

5—Add 5 cc. Schiff-Elvove reagent, mix well, and let stand till colors are sufficiently developed (0.5 to 2 hrs.).

Each 1 cc. of the 0.04 per cent. methanol in the standard tubes is equivalent to volume percentages of methanol in total alcohol contained in the sample as follows:

Sample Solution	*Per Cent.*
A	1
B	5
C	25

For more precise results the determination is repeated on the appropriate sample solution with more closely set standards. The sharpest results are obtained with standard tubes containing not over 1 cc. of standard methanol. To bring the sample into this range it is often best to use only 2 cc. of a sample solution, adding

thereto 0.5 cc. of the 4 per cent. ethyl alcohol and sufficient water to make 4 cc. Approximate readings may be made after 30 minutes, precise ones after 1 hour, but best under 2 hours, for the colors fade later. The limit of detection is 0.2 cc. of the standard 0.04 per cent. methanol.

Tests on four "unknown" mixtures of methanol, ethyl alcohol, and water prepared by an assistant indicated that, including the necessary determination of total alcohol via specific gravity, the results need not be in error by more than 1 part in 20.

QUALITATIVE METHOD.

A modification of Denigès' method is official as a qualitative test in the U. S. Pharmacopeia IX. The U. S. P. test has been criticized as unreliable because a false reaction sometimes occurs. Ehman[8] attributes the fault to temperature and overcomes it by running a blank with pure ethyl alcohol, adjusting the temperature until the blank remains colorless. In the judgment of the present writer the difficulty is primarily due to an undesirably high concentration of total alcohol. Since the substitution of phosphorio acid for sulfuric acid considerably more than doubles the yield of formaldehyde from a given amount of methanol, the concentration of the sample in the test here proposed need be only half that employed in the U. S. P. test and still leave the proposed test more delicate than the U. S. P. test at its best. The proposed test has been run at temperatures of 15° and 35° C. without experiencing difficulty with false reactions.[9] It may be conducted as follows:

Dilute the liquid, purified as necessary, to a content of 5 per cent. by volume of total alcohol. To 5 cc. add 0.3 cc. of phosphoric acid (C. P.; 85 per cent.) mix, add 2 cc. of a 3 per cent. solution of potassium permanganate mix and let stand until the permanganate is entirely decomposed (about 10 min.). Add 1 cc. of 10 per cent. oxalic acid mix, and let stand till a clear brown (about 2 min.). Add 1 cc. concentrated sulfuric acid, mix, add 5 cc. Schiff-Elvove reagent, immediately mix well, and observe the color after exactly 10 min. The solution may then possess a pale greenish tint, but should show no distinct blue or violet color against a white background (less than 0.2 per cent, methanol in the total alcohol).

[8] *Am. J. Pharm.*, 91 (1919), 594.

[9] It may be that in the U. S. P. test the presence of sulfuric acid promotes oxidation of ethyl alcohol to formaldehyde at an elevated temperature.

In carrying out the qualitative test it is essential not to be misled by any colors developing in less than 10 min. Concentrated sufluric acid often becomes decidedly weak in the ordinary laboratory reagent bottle, and a transitory color from acetaldehyde may accordingly appear. This is also likely to happen if the Schiff-Elvove reagent is not mixed with the solution immediately after addition. The color arising from acetaldehyde will have disappeared in 10 min. after mixing, but, needless to say, it is a safeguard against error to run a blank along with the test. On longer standing, the test can naturally detect smaller proportions than 0.2 per cent.

PURIFICATION OF SAMPLES.

The directions given for both quantitative and qualitative work specify that the original material must be "purified as necessary." In general, the test must never be run directly on any material unless it is positively known to contain only water, alcohol, and other substances known to be innocuous. Alcoholic preparations vary so widely that no entirely general methods of purification may be given. The analyst can generally determine approximately the nature and amount of the non-alcoholic constituents, and must decide whether, in addition to purification, it will be necessary to run a blank on a synthetic mixture.

Carbohydrates and Glycerol—These substances, against which Salkowski[10] has given warning, are to be separated by distillation; a step which is also necessary to permit determination of total alcohol via specific gravity.

Formic and Acetic Acids—These acids are stated by Rosenthaler[11] to yield color with Schiff's reagent. They can be separated, if necessary, by distillation after neutralization, but the present writer did not find that 10 per cent. by volume of either acid added to pure ethyl alcohol produced any color by the qualitative test.

Formaldehyde, Terpenes, Etc.—These impurities are removed by von Fellenberg[12] by treatment with sodium hydroxide and silver nitrate, followed by distillation.

[10] *Z. Nahr.-Genussm.*, 28 (1914), 225.
[11] "Der Nachweis organischer Verbindungen," 1914.
[12] *Biochem. Z.*, 85 (1918), 45.

Phenol—As noted by Scudder,[13] phenol interferes with the test to a degree dependent on its concentration. It may probably be adequately separated by distillation after addition of a liberal excess of caustic alkali.

Fusel Oil—This has been stated[14] to afford a slight false reaction after oxidation. The present writer obtained one sample of "fusel oil," and two of C. P. amyl alcohol (rectified fusel oil), one of the latter being an "analyzed reagent," all from different manufacturers. Each sample was made into a 10 volume-per cent. solution in pure ethyl alcohol, and the qualitative test was applied. The heaviest color was given by the presumably purest sample, namely, the "analyzed reagent." Upon making the qualitative test quantitative by running it in comparison with known mixtures of methanol and ethyl alcohol and letting stand an hour or more, the color produced was found markedly fainter than the color produced from ethyl alcohol containing 0.08 per cent. methanol. By the regular quantitative test the color was indistinguishable, being clearly less than the equivalent of 0.1 per cent. methanol. Hence the present writer has been unable to demonstrate interference by fusel oil, provided that it be not attempted to strain the test beyond the limit recommended, namely, 0.2 per cent.

Acetone—This ingredient, constituting up to 10 per cent. of the "total alcohol," does not appear to affect significantly qualitative or quantitative results.

SUMMARY.

The Denigès test has been modified to increase sensitiveness and precision, and is recommended for practical work in the detection of, and especially in the quantitative determination of, methanol in the presence of ethyl alcohol, inasmuch as the possible normal presence of methanol in alcoholic products renders purely qualitative tests unsatisfactory. Though capable of greater refinement, the tests are adjusted to a minimum limit of 0.2 per cent. methanol in total alcohol. Procedures for the removal of certain interfering substances are outlined.

[13] *J. Am. Chem. Soc.*, 27 (1905), 842.

[14] von Fellenberg, *Biochem. Z.*, 85 (1918), 45; Salkowski, *Z. Nahr.-Genussm.*, 36 (1918), 262.

A HALF CENTURY OF AMERICAN PHARMACY.*

(Address of Prof. H. V. Arny, Columbia University, at the Jubilee Celebration of the Ontario College of Pharmacy.)

It is a great honor and privilege to bring to the Ontario College of Pharmacy upon this memorable occasion the greetings of the pharmacists on the other side of the Great Lakes. The name "Canadian" has taken on new meaning to us living under the Stars and Stripes since your brave sons fought on Vimy Ridge and reddened even the poppies on Flanders fields. With naught but the St. Lawrence, the Lakes and a few thousand miles of imaginary line separating us, our countries, peaceful neighbors for over a century, became comrades in arms for eighteen of the War's fifty-one tragically glorious months; so soon, alas! forgotten in certain quarters.

To refer to the occasion we celebrate, it is a great thing for an organization to have weathered the changes and chances of half a century. It is a matter worthy of the most cordial congratulations that this organization has attained the vigorous fifties with so fine a record of achievement. May the coming fifty years of the Ontario College of Pharmacy be of even greater success than the half century just drawing to a close.

We pharmacists in "The States" have been celebrating to quite an extent during the past year. Just one year ago the oldest State Pharmaceutical Association, that of New Jersey, celebrated its semicentennial, while this very week, the oldest College of Pharmacy in America, that in Philadelphia, is holding its one hundredth graduating exercises.

Since 1920-21 has been a year of celebrations, it is well to pause a few moments to look back over fifty years with the hope of gaining from the past lessons for the future. Pharmacy has been far from quiet during this half century. Let us see whether its activities have been for good or evil.

Let us imagine ourselves back in 1871 when the Ontario College of Pharmacy was organized. My childhood memories of the seventies hover around a fine old town at the other end of the country from whence I come, New Orleans; washed by the Father of

*From *Canadian Pharmaceutical Jour.*, July, 1921.

Waters, and fanned by the breezes from the Gulf of Mexico. Far away though it is, I doubt whether the drug business down there was much different from that plied up here. I recall a fine old druggist named Pope, with a choice store in a select neighborhood. An attractive store it was, with white wall fixtures upon the shelves of which were rows of bottles with gold labels bearing mystic names; with narrow white counters surmounted by small show cases made of panes of ordinary glass, fastened together by wooden frames; with the dispensing counter and the soda counter possessing the "novelty" of marble slabs; with a soda fountain made of marble, shaped like a cottage, or a barn. In the rear there was a room from whence mysterious noises and still more mysterious odors proceeded; the noise of the clanging pestle against the iron mortar, a symphony I was destined to produce many times a decade or so later; the odor of wild cherry, of aloes, of turpentine and of valerian. There was another drug store, that of Dr. Hastings, that enthralled me still more, for from it proceeded an odor that blended all of the mystery of centuries of incantation and drug magic. The memory of that odor clung to me until my student days; when delving in the stinks of chemistry, I recognize my old friend of the Hastings pharmacy in *Mercaptane*. Here is a clue for the pharmaceutical historian. Did Dr. Hastings anticipate sulphonal and its congeners? Before the historian goes too far in this quest, I might add that I understand that Dr. Hastings had installed upon his premises an apparatus for making his own illuminating gas.

Then there was in New Orleans in the seventies the drug store of Thomas Finlay, a well-trained pharmacist, the great prescriptionist of the English-speaking medical men; a store from whence sprang his nephew, Alexander K. Finlay, thirty-ninth president of the American Pharmaceutical Association. Across Canal Street, the mystic line separating the New Orleans from the old; in the old French quarter famed in song and story, there were *pharmaciens* of ability and of worth; there were drug stores that rarely came before the eyes of the American boy now telling you the story. There were Laplace, Cusach and Robin, leaders among their pharmaceutical *confreres*.

And now to jump from the Gulf to the Lakes, from the land of the palmetto to the land of the maple, I leave to you, who know better than I, the picturing of those goodly men of the Province of

Ontario who founded your college; blood brothers of the Popes, the Hastings and the Finlays of far-off New Orleans. Of these worthies the one whom we of the United States hold in grateful remembrance was your William Saunders who, in 1871, was active in manufacturing pharmacy; a constant exemplar of the fact that a pharmacist is an educated man. Twenty-fifth president of the American Pharmaceutical Association, Dr. Saunders has always seemed to us of the United States, the personification of Canadian Pharmacy. Others there are, to be sure, to whom we turn with like esteem, but since some of them are present tonight, I will spare their feelings by permitting the name of Dr. Saunders to stand alone.

From the apothecaries of 1871 let us turn to the pharmacy of the same period. In these days the art of dispensing meant more than it does in the drug store of 1921. The spreading of plasters was an every-day occurrence, and apothecaries took pride in showing their skill in preparing those of unusual shape. Machine-spread porous plasters brought out in 1847 by one patent medicine manufacturer, were still novelties from the dispensing standpoint in 1871. Pills were made by hand by the druggists in quantity lots. Even thirty-seven years ago, when I began my pharmaceutical apprenticeship, we made all of the pills (such as compound cathartic and quinine) that were sold over the counter; the only coated pills we dispensed being proprietaries or special lines prescribed by physicians because of the advertising activity of their manufacturers. Compressed tablets, introduced into American Pharmacy by Jacob Dunton, of Philadelphia, during the late sixties, were being pushed by a few manufacturers but were dispensed by apothecaries only upon the prescription of the physician who specified them. Tinctures were the staple form of drug medication; fluid extracts being then new and of lesser importance. Mixtures were prescribed largely and were freshly prepared by the apothecary. Malodorous milk of asafœtida and its sinister sister, Dewee's Carminative, were in great demand, and a fine job it was to make the former when one, all dressed up, on one's Sunday off, came back to relieve the employer or the brother clerk over the dinner hour. Emulsions of fixed oil were in their infancy a few stray recipes for cod liver oil cream being found in the literature of 1870-71. Elixirs were then in their first flush of popularity, with those dispensing them little

dreaming that within a half century they would command the attention of Prohibition officials. Hypodermic medication was an entire novelty that was much discussed in the journals of half a century ago, and it is obvious that serum medication was unknown; in fact the word "antiseptic" was used but seldom and "the new germ theory of disease" was the subject of an address before the British Association in 1870.

As to drugs, eucalyptus was a novelty; while cascara-sagrada was unknown; strophanthus was of interest only as an African arrow poison. In the chemical field, among the "new medicines" we find chloral, phenolsulphates and potassium permangate. The German tar barrel had not yet started to turn out antipyretics and hypnotics and antiseptics for the healing of nations and for the filling of German purses. Phenol, of course, was used, the famous brand of that time being that of the English house of Calvert, who brought forth their first pure product in 1863.

Medical thought of half a century since was immensely different from that of today. With the germ theory in its infancy, with antisepsis merely a matter of chance, with toxins and antitoxins unknown, the physician had to depend upon drugs and chemicals and that, it must be admitted, in a rather hit or miss fashion. Homœoapthy was under serious discussion, both in the English and American pharmaceutical press; since it was viewed both by the regular physician and by the apothecary with a feeling akin to alarm. The Hahnemannian school has exerted considerable influence, although not in the way that was anticipated in 1871. It had its part in turning physicians of the regular school from the nauseatingly bitter mixtures of those days to more palatable preparations; it had its effect in persuading the old line medical men that reasonably small doses frequently repeated are often of more service than the occasional administration of heroic doses; it may have inspired the therapeutic nihilism of the ultra-modern teachers of medicine; a philosophy the logical sequences of which are the healing cults such as Eddyism.

Whatever its influence upon the regular practice of medicine, homœopathy has had a decided effect upon the practice of pharmacy. Practitioners of the regular school, feeling the competition of the homœopathic physician with his satchel of sugar pills, began dispensing instead of writing prescriptions. The tablet industry, in

its infancy in 1871, has, during the half century since that time, assumed enormous proportion in supplying the needs of the average dispensing physician and tablets have now become as staple as ground flaxseed. If the tablet vogue continues there may be some day an automat, doctors and druggists rolled into one, in the form of a nickel-in-the-slot machine, dealing out tablets for all sorts of ailments. Already around New York tin boxes containing a well-known brand of acetylsalicylic acid tablets are being sold at newsstands. With the lessening of the prescription business the pharmacist has had to turn to other means of paying his constantly increasing rent and as a result, in the cities at least, the old-fashioned drug store has given place to a handsome emporium in which the dispensing of medicine seems the least part of the business. And then, forsooth! the physician, intentionally overlooking the causes of the commercialization of pharmacy, throws up his hands in holy horror over the modern drug store and thus justifies his neglect of the art of prescription writing.

This is the situation, but that it is not so gloomy as the pessimist may think, the presence of you prosperous gentlemen at the semi-centennial of your organization seems to attest. Nor do I believe that your prosperity has been due solely to the sale of apples, of cameras and of sandwiches. The remarkable growth of schools of pharmacy, including your own fine institution, shows that there still remains an art of pharmacy, a science of pharmacy, and a profession of pharmacy. Did I not think so I would consider that I was obtaining money under false pretenses in accepting my salary as teacher, and I would turn to the business of pharmacy rather than remain in the ranks of the teachers.

We have considered the past and the present of pharmacy. How about the future of Pharmacy? I am an optimist and can say with Rabbi Ben Ezra:

> "Grow old with me
> The best is yet to be,"

and so I have no fear that the future will see relegation of pharmacy to the things of the past along with astrology, alchemy and necromancy.

That a man of indifferent education and mediocre ideals will be naught but a tradesman in pharmacy, even as an indifferent

farmer will be naught but a hewer of wood, a drawer of water and a digger of ditches, goes without saying. But if a pharmacist has the vision, not necessarily of "The Gleam" that Tennyson writes about, but a view of the broad expanses of opportunity before him, that man will not only be an exponent of real pharmacy, but will also be a successful pharmacist.

Let me give a few illustrations of what I mean. Here is one pharmacist I know who is famed in the city where he lives as having the one apothecary shop where all sorts of finely garbled herbs are available; not the compressed packaged herbs that are seen in most stores, but carefully dried herbs almost as handsome as herbarium specimens.

Here is another retail pharmacist, a Bell scholar, by the way, who is gaining reputation throughout the United States for the digitalis preparations standardized by the Hatcher method.

Here is a Southern druggist who, having a bent toward chemistry, specialized in making unlisted chemicals for those physicians desiring them, thereby adding to his daily receipts and to his reputation among the medical fraternity.

Here is a New York pharmacist who dared to specialize as a prescriptionist, who prepared himself to dispense sterile medicaments in ampule form, and who now has people coming to his store from all over the big city, asking for special prescription work of highly technical character; ready to pay the adequately high price that such service means.

Here is an apothecary in a city on the Great Lakes, who, despite the enormous number of thyroid preparations on the market, has built up quite a business in dispensing, in capsules, dessicated thyroids sent to him in fresh condition from the slaughter house. It is needless to say that this man has the finest prescription business in his city.

Here is the pharmacist (now numbered by scores) who, starting in by performing in a satisfactory manner urinary work for the medical profession, has developed that side-line into a busy laboratory where the chemical and bacteriological side of clinical diagnosis is performed at fees commensurate with the service.

And lastly, let me cite by name one pharmacist, who showed us of the United States, the possibilties of professional pharmacy, that great pharmacist, Henry P. Hynson, of Baltimore, whose de-

mise on the 19th of last April brought sorrow to all of his co-workers in the American Pharmaceutical Association. No higher tribute can be paid Dr. Hynson than the following paragraph taken from an editorial published in a recent number of the *Journal of the American Medical Association:*

"As already suggested, his constant effort was to emphasize as of primary importance the service which the educated scientific pharmacist was in a position to render to the public, and to decry the commercial ideas which seemed to be strangling the professional instincts of the pharmacists. He opposed commercial drug store exploitation of the public with 'patent medicines' and making pharmacy a mere adjacent to the sale of soda water, light lunches and novelties. Hynson was one of the few prominent pharmacists who were willing to forego financial gain in order to raise the ethical standards of a profession which he honored. He took an earnest interest in all the live pharmaceutical questions of the day, and pure pharmacy sustained a great loss in his death."

THE RELATIVE VALUE OF THE PROTEINS IN NUTRITION.*

By R. H. A. Plimmer.

Complete hydrolysis of the protein to its constituent 18 or 20 amino-acids occurs during digestion in animals; the amino-acids circulate in the blood and reach the various organs, which build up new tissue from the units. Animals have been maintained on a diet containing as its protein content a mixture of pure amino-acids in suitable proportions. Biologically, the proteins must therefore be regarded as mixtures of the various amino-acids, digestion and absorption as a re-shuffling of the units. The amino-acids are not convertible into one another, nor capable of being synthesised by the animal organism, with the exception of glycine, which, under certain conditions, can be formed in the body. The different proteins have different compositions, thus, for example, casein contains 16 per cent. of glutamic acid and gliadin 40 per cent. Some proteins are complete, *i. e.*, contain all the amino-acids, others are incomplete and lack certain units. It can thus hardly be expected that proteins should have the same value in nutrition. Some of the

*From *Journ. Soc. Chem.* Ind. June 30, 1921.

amino-acids may be indispensable, others not so essential. There are two main problems to study in nutrition: the formation of new tissue, as in the growth of young animals, and the maintenance of tissue, which undergoes so-called wear and tear, in adult animals. The problem is ultimately to find out the function of each amino-acid in growth and maintenance.

THE EFFECT OF THE ABSENCE OF CERTAIN AMINO-ACIDS.

The most certain way of studying the problem is to feed animals upon known mixtures of amino-acids, but the practical difficulties are far too great. The amino-acids are not easily prepared, and it is almost impossible to obtain sufficient of each of them to feed an animal, even a mouse, for any length of time. Two other ways are possible:—(a) To feed incomplete proteins and add the missing unit or units; (b) to feed completely hydrolysed proteins, *i. e.*, a mixture of amino-acids from which one or more units have been removed by chemical means.

The first experiment of this kind was made by Willcock and Hopkins in 1906. Zein was chosen as incomplete protein and fed to mice: in one set alone, in another set with the addition of 2 per cent. of its amount of tryptophan. Failure occurred in both sets of animals, but not so rapidly in those on zein and tryptophan. Young mice with zein alone died generally in 16 days; with zein and tryptophan in 30 days. Adult mice without tryptophan lived 27 days, with tryptophan 49 days. The survival period was thus appreciably lengthened by the presence of tryptophan. The failure to live was most probably due to the absence of other units from the zein. Ackroyd and Hopkins repeated the experiment in 1916 by the second method of experimenting which offers better conditions. The animals were fed upon a mixture of the amino-acids from casein. This mixture does not contain tryptophan, since it is destroyed by acid hydrolysis. In the first period tryptophan was added; on the twelfth day it was omitted and introduced once more on the thirty-fifth day. The animals continued their growth during the first period, declined in weight during the second period, and grew again in the third period when the tryptophan was present.

Osborne and Mendel in America have made numerous experiments with various pure isolated proteins of known amino-acid composition. Their most important results in this connection were

with wheat gliadin; this is a complete protein, but has very little lysine. Adult rats were maintained for long periods on this protein—as long as 500 days—but young rats, though they lived for long periods, failed to grow. The authors therefore regarded lysine as essential for growth. Later, they showed that if they added lysine at definite intervals to the food containing gliadin as sole protein, growth took place with the lysine, but not without it. The minimum amount of lysine necessary to produce normal growth was found to be between 2 and 3 per cent. of the amount of protein in the diet.

The value of lysine for growth was shown in a more practical way by Buckner, Nollau and Kastle. They fed chickens on a poultry farm on diets of high and low lysine content. Their figures and photographs definitely showed more rapid growth on the mixture of high lysine content.

The two other hexone bases—arginine and histidine—are essential units of proteins. As shown by Ackroyd and Hopkins, their removal from the hydrolysed casein mixture leads to loss of weight of the animals; if only one is absent from the food the rate of growth is lessened, so that it appears as if these two units were inter-related. The structural formulæ of these compounds suggest a possibility of the conversion of the one into the other by the wonderful mechanisms of the animal body. These two units were found to give an increase of allantoin in the urine of the animals; thus we know that the purine ring can be synthesised from them. This synthesis by animals has long been suspected, as young birds and animals produce purines on a diet with an almost complete absence of purine compounds.

It is more difficult to arrive at the function of the amino-acids containing aromatic nuclei. Some proteins lack tyrosine, but all contain phenylalanine, which is very difficult to remove from a mixture. Phenylalanine and tyrosine both give rise to homogentisic acid in cases of *alkaptonuria;* phenylalanine may therefore be oxidisable to tyrosine in the body. The almost complete removal of tyrosine from the mixture from casein made no difference to the growth of rats, as shown by Totani. The amount of phenylalanine in the mixture was thus probably sufficient to supply the need for aromatic nuclei. According to Abderhalden, tyrosine cannot be dispensed with.

Cystine is the only unit which contains the element sulphur, though another sulphur-containing compound may be present in proteins. The amount of cystine is not known except in a few cases, but it is estimated from the sulphur content. The need of cystine in the food has been shown most conclusively by experiments with phaseolin, the protein of the navy bean. Slow growth resulted on a diet with the protein alone, but normal growth followed the addition of 2 per cent. of its amount of cystine. Very little sulphur is present in casein. Osborne and Mendel found that less casein was required in a diet if it were augmented with cystine: 15 per cent. casein alone gave normal growth, but 9 per cent. if cystine were added.

It is not possible to test a protein without proline, but arachin with only 1.4 per cent. was tried by Sure. This protein failed to give normal growth even after the addition of extra proline, so that its deficiency must be caused by another missing substance. It is possible that proline and glutamic acid are related units in the molecules of the proteins.

An experiment has also been made to see if the animal organism can introduce an amino group into the molecule of nor-leucine and convert it into lysine. Animals fed upon gliadin and nor-leucine did not grow just as on gliadin alone. The synthesis is thus not possible.

The whole group of simple mono-amino-acids has yet to be tested. They may not all be necessary. In cases of diabetes several can give rise to glucose; their function may be to supply energy through their conversion into sugar. Isoleucine is absent from gelatin, as recently shown by Dakin; this may be another reason for the failure of gelatin in nutrition, which is usually attributed to the absence of tyrosine, cystine and tryptophan.

COMPARATIVE NUTRITIVE VALUE OF PROTEINS.

Few proteins show such marked deficiencies as gelatin, gliadin and zein. The different amounts of the units in complete proteins make little difference to growth if the diet contain *abundance* of protein. Growth is observed on the most varied proteins of animal and plant origin; but if any *restriction* in the amount of protein in the food be made, then the growth is lessened or inhibited. Each complete protein will thus have a definite minimum for growth.

Two per cent. lactalbumin gave maintenance, 4.5 per cent. growth; 2 per cent. edestin scarcely gave maintenance, 4.5 per cent. slight growth; with other proteins 2 per cent. led to loss of weight. With a protein content of 4.5 per cent. the best growth was with lactalbumin, followed by edestin; there was no growth with casein unless supplemented with cystine, or with glycinin or squash-seed globulin. An experiment showed that a food with 9 per cent. of lactalbumin was equal to one with 12 per cent. of casein or with 15 per cent. of edestin.

THE NUTRITIVE VALUE OF THE PROTEINS OF LEGUMES, NUTS, ETC.

The legumes contain large amounts of protein, and the chemical analysis of the proteins shows no abnormality. The proteins of the pea have been found inadequate by McCollum; it is probably due to lack of cystine, for, as stated above, phaseolin is supplemented by cystine.

The soya-bean protein is of good quality for normal growth, so also are the proteins of the peanut. The latter are peculiar in their high lysine content. The proteins of these foods require cooking so as to make them capable of being digested and assimilated.

The edestin of hemp-seed and cotton-seed is not a perfect protein with its high arginine and glutamic-acid content, but the foodstuff is largely used in America as cattle food. Its poisonous constituent can be removed by steaming or by the hot method of oil extraction.

Nut proteins have a high value on account of the high proportion of hexone bases which they contain. Normal growth has been observed on coconut press-cake, walnut, filbert, pine nut, and other nuts. Experimental work has thus confirmed the assertion of fruitarians of the high value of nuts in nutrition.

THE NUTRITIVE VALUE OF THE MIXTURE OF PROTEINS IN CEREALS.

Though the gliadin group of proteins of cereals is not adequate as source of protein in the food, it does not follow that the mixture of proteins in the grain is likewise insufficient. Wheat and maize glutenins as sole protein have been found satisfactory for growth, and may compensate for the inefficiency of the gliadins. The whole grain contains also small quantities of an albumin, globulins, and proteose. Particular attention has been paid to the nutritive value of cereals. The results are not altogether consistent; the

discrepancies seem to be due to the different basal diets used by the various investigators. The results of McCollum and associates are very contradictory; they believe the inadequacy depends on improper mineral supply. Insufficiency of vitamin supply is a contributory cause. Osborne and Mendel tried not only the whole grain, but also different commercial articles produced by milling, such as wheat flour, bran, embryo. Normal growth followed the use of whole grain, and very little difference was noticed among the various grains.

In all cases animals kept for long periods produced small or no litters of young; their health had thus been impaired. This loss of reproductive power has been observed by all workers if cereals supply the sole protein.

Wheat embryo contains the albumin, and is fully adequate; bran proteins are even of superior value. Wheat flour, pearl barley, and maize meal are not adequate.

The milling process thus removes "good" protein. Wheat flour, etc., does not contain enough total protein, but in the experiments the total was made up by adding gluten. The endosperm of the grain will only furnish protein for maintenance.

SUPPLEMENTS TO THE PROTEINS OF CEREALS.

Neither men nor animals consume the whole cereal, and as the endosperm does not supply enough protein in quantity or quality, it must be supplemented. The protein ratio of 1 : 10 needs to be increased up to 1 : 5. Animal proteins form the best supplements. Lactalbumin was shown by Osborne and Mendel to be the best supplement, but for some peculiar and unaccountable reason other workers do not find this protein so good. Meat, milk, eggs are almost equally efficient, but casein is of less value. In the case of maize meal and milk at least an equal part of skim milk is needed; this gives 30 per cent. of the mixture of proteins as derived from milk. Yeast protein and peanut flour are good supplements. Cottonseed and pea are inferior, whilst products like distillers' grain or vegetable albumin, which is derived from grain, are of little value. The best supplementing proteins are thus those containing the hexone bases, tryptophan, etc. which are low in amount in the cereals.

To produce normal or rapid growth it is possible that it may be more economical to use "good" proteins, which are more expensive than "bad" proteins.

QUALITY OF PROTEIN IN MILK PRODUCTION.

Diet plays a large part in milk production. Quantity and quality of protein are the chief factors. Since neither the animal body nor the mammary gland can synthesize amino-acids, the food must contain sufficient for the manufacture of casein and lactalbumin. Hart and Humphrey have paid some attention to this question. A high milk yield of 27 lb. requires a protein ration 1:4.5; 1:6.7 is necessary for 11 lb.; 1:8.5 is not economical. If the animal is not furnished with sufficient protein it produces milk from its own tissues. Skim milk has an efficiency of 65, against 25 of a mixture of maize and alfalfa. Gluten feed (maize embryo) has 45, flax seed 61, casein 59, milk powder 60. A comparison of clover and alfalfa on the same basal diet showed a superiority of alfalfa for high milk production for 16 weeks. With another basal diet the reverse may be the case. The value will depend on the proportions of the amino-acids in the food and their correspondence to the proportions in the milk proteins. No guide is at present available from the side of chemical analysis. Little is known of the proteins of grasses and green foods. The nearest approach to the proteins of cow's milk are the proteins contained in the milk of other animals. If the milk proteins of all animals are the same in composition, the milk of one animal will be as good as that of another animal,. but if not, as is most likely, the best source is the animal's own milk. Cannibalism has been proved to be the best method of feeding dogs. We approach cannibalism in the nursing of the young on mother's milk. Milk contains ultimately the proteins of the mammary gland.

PROTEINS AND PELLAGRA.

The primary cause of the disease pellagra appears to be quality of protein, but at the same time insufficiency of protein together with improper salt supply may play a part.

Pellagra was not recorded in Europe before the introduction of maize into Spain by Columbus. The disease spread to France, Lombardy and eastwards, wherever maize was extensively used for food. Roussel (1866) cured it by good food, and advanced cases have been successfully treated by a generous diet (Lorentz, 1914; Willets, 1915). Goldberger cured and prevented the seasonal appearance of pellagra in lunatic asylums by increasing the meat and milk in the diet, which had previously been very deficient in this

respect. Goldberger produced the disease experimentally in a squad of volunteers by a diet consisting of vegetable protein, mainly wheat, maize and rice. On a vegetable diet principally of maize, Chick and Hume produced symptoms in monkeys very like the symptoms of pellagra in man, and a cure was effected in one case by a diet containing better proteins.

Wilson, of Cairo, who investigated the outbreaks of pellagra in Armenian refugee camps at Port Said, found the diet was inadequate in energy supply and protein supply (vegetable). Thomas (1909) tested the comparitive values of proteins for man, and found that meat was three times as good as maize. Wilson, calculating from Thomas' figures, determined that the refugees had a casein equivalent of 22 gm. per day. On improving to a casein equivalent of 41 gm. per day no more cases of pellagra occurred. Shortage of protein and quality of protein are thus at the root of the trouble.

AN IMPROVED METHOD OF PRESERVING SPECIMENS FOR A HERBARIUM.*

By E. A. Price and Noel L. Allport.

The procedure generally adopted for the preservation of botanical specimens leaves much to be desired. The flowers are simply introduced between sheets of absorbent material, such as blotting-paper, and subjected to pressure, either in books or the botanical press. The process is long and tedious, requiring not less than three weeks to complete; it necessitates repeated changing of the absorbent sheets, and since the tissues become flimsy the risk of distortion is very great; in wet weather the plants must be first freed from external moisture; finally there is the liability to infection by mould. Even when these difficulties are overcome the resulting specimens lack permanence, both of shape and color. Particularly is this the case with members of the *Orchidaceæ,* which become wrinkled and assume a dirty brown tint; again, aquatic plants, such as *Hottonia palustris,* cannot be induced to retain the delicate coloring of the leaves and flowers.

*From *Pharm. Jour. and Pharm.*, July 2, 1921.

THE IMPROVED METHOD.

The improved method about to be described, while being exceedingly simple and calling for no elaborate apparatus, is free from almost all the disadvantages cited above. About one and a half hours will usually suffice to complete the whole operation; the characters of the flowers, including the delicate gradations of color, are permanently preserved; the actual manipulation of the process is much easier than is that of the old method; and after a little practice the procedure can be relied upon to work on all occasions. It may be particularly noted here that the different shades of green in the leaves, which are so rarely maintained in their true contrasts, are satisfactorily preserved in collections treated in this way.

The plant is first placed between about twelve sheets of white blotting-paper, so that there are six sheets above and below. It is then gently pressed with a moderately warm domestic flat-iron of about two pounds weight. The iron should be kept constantly moving. The temperature of the iron is, of course, an important consideration. The best gauge is experience. If the metal is too hot the coloring matters of the plant, particularly the chlorophyll, will be decomposed, and the specimens thus rendered useless. On the other hand, if the temperature is inadequate the permanency is impaired and the plant becomes brown; this is possibly due to the fact that the contained enzymes have not been inactivated. As a rule the growth of enzymes is rapidly inhibited by exposure to a temperature of 70° C. The heat applied should be sufficient to cause water vapor to rise through the blotting-paper as the moisture of the plant is dried out. We suggest that 110° C. would not be very far wrong. Floral collections thus treated are no longer flimsy, but dry and rigid, yet otherwise retaining their natural appearance. The liability of the blotting-paper containing chemical impurities with disturbing influences is not great, but it should, nevertheless, be recognized as a possibility. All paper is bleached with calcium hypochlorite, and if any traces should remain in the material used for pressing plants the colors of the tissues may be altered. If any trouble is met with in this direction another brand of paper should be tried.

Immedaitely after preservation in this manner the specimens should be painted over with a dilute solution of mercuric chloride in absolute alcohol, a suitable strength being about 0.5 per cent. This

will render them impervious to attack by parasitic insects and moulds. It will not be appropriate to offer a few observations on the mounting of the plants. The most satisfactory support is Whatman's thick, white cartridge paper, such as is used by artists for sketching. The ordinary gum of commerce frequently contains sulphurous acid added as a preservative, and should therefore not be employed as an adhesive, since it is liable to bleach the plant colors. The best mountant is a mucilage of the pure gum acacia of the B. P. to which has been added a few grains of Beta-naphthol to prevent its decomposition. This preparation has the advantage of being free from chemical impurities, is firmly adhesive, and is invisible. It will be shown later that it is sometimes advisable to divide a plant into its component parts before preserving, and where this has been done the general rule for mounting is to fix the main axis and foliage leaves to the paper support first, then the inflorescences can be easily fitted in their correct positions. The tissues being strong and inflexible after the preservation treatment, there is no difficulty in reassembling the parts. Dissections illustrating the constructional characteristics may be mounted beside the complete plant. The liability of these component parts to fade and crinkle is avoided by the new method, thus overcoming a time-honored difficulty. Thus, excellent illustrations of the primrose can be made exhibiting the pin-eyed and thrum-eyed varieties and their adaptability to cross-fertilization. It was noticed that when this ironing process is employed the liability of the dissections going green is obviated. With large flowers and leaves the adhesive may be applied to the back of the plant itself, while for small examples it should be spread on the paper only. When the paste has been applied and the specimen fixed in position it should be firmly pressed with a soft cloth to ensure the removal of air bubbles which tend to form under the leaves, and if ignored at this stage will give the plant a wrinkled appearance when it is dry. We possess a collection preserved and mounted as detailed above that has retained the color of both flower and foliage during a period of eight years.

Certain orders of plants demand special treatment to which our process is readily applicable. A few examples will be mentioned and will serve to demonstrate the practical possibilities of the method.

COMPOSITÆ.

It is necessary with flowers of this order to gently flatten the disc florets to the same level as the ray florets by applying the apex of the flat-iron to the former before giving the general pressure to the whole specimen; otherwise, of course, the ray florets will be shrivelled.

ORCHIDACEÆ.

As is well known, these flowers consist of massive tissue, and it is often advisable to remove the perianths and press them separately. They can all be detached first by cutting across the ovary and then mounted on to the remainder of the plant afterwards. With the exercise of a little care it is impossible to detect that any separation has been made. Such specimens as *Ophrys apifera, Ophrys muscifera, Cypripedium calceolus* and *Listera cordata* can thus be preserved with every detail of their natural color permanently retained, which is extremely difficult, if not impossible, by the old method. It may be noted generally that in all big flowers the preservation of the smooth texture and natural color of the corolla, or perianth, is greatly facilitated by dividing from the main axis, then preserving and mounting separately.

SPECIAL FLOWERS.

Such special flowers as *Drosera rotundifolia* and *Pinguicula vulgaris* respond admirably to the ironing process. It is possible to preserve them with the insects caught by the plants, *in situ*. If the leaves of the former are treated separately, specimens can be prepared demonstrating the glands bent over towards the insect situated on the leaf surface; at the same time the delicate shades of red and green are retained. In preserving a plant such as the *Paris quadrifolia,* the advantages of the new process are very manifest. By the original methods the contrasting greens become a dull monochrome, whereas it is possible by the procedure described to permanently preserve the delicate greens of the perianth, the yellow anthers, and the shades of purple in the ovary and stigmas.

VIOLACEÆ AND IRIDACEÆ.

Some plants, such as most members of the *Violaceæ* and *Iridaceæ* will probably lose their color quite irrespective of the method employed. The plants, after this new treatment, are, however, so hard and firm that a way of overcoming the difficulty was found.

After preserving and mounting as described, the coloring matter from several flowers of the same species was extracted with absolute alcohol, and the liquid thus obtained was used to paint the specimen intended for the herbarium. In this manner an example of *Iris pseudacorus* has the appearance of having actually retained its yellow color.

In conclusion, we would commend this new method to those who have suffered many disappointments in endeavoring to make a satisfactory herbarium by the old system of continued pressing. The process here explained has been tried and proved, and we are able to claim for it that it not only gives more gratifying results, but that it is also easier to manipulate.

THE TITRATION OF CERTAIN ALKALOIDS.*

By Norman Evers, B. Sc., F. I. C.

In examining the literature of analytical chemistry in the light of modern development of the theory of titrations one is struck by the haphazard way in which indicators are recommended for titrations. Most frequently indicators appear to have been chosen on account of the sharpness of the end-point rather than on account of suitability on theoretical grounds for the titration in question. Further, the indicators used are chiefly confined to methyl orange, phenolphthalein, litmus, and cochineal no one of which, with the exception of phenolphthalein, can be regarded as a good indicator when compared with the new and brilliant indicators which are now available. Probably the chief reason why these new indicators are not in more common use is the absence of any data as to the titrations to which they are applicable.

THEORETICAL CONSIDERATIONS.

In a theoretically perfect titration of a weak base, such as morphine, we should run in standard hydrochloric acid until we had in our solution nothing but pure morphine hydrochloride. The means by which we determine when the morphine is in the state of hydrochloride is by adding an indicator. Now all indicators change

*From *Pharm. Jour. and Pharm.*, June 18, 1921.

in color over a definite range of hydrogen ion concentration—that is to say, the change of color of an indicator is brought about by hydrogen ions, and what we are actually doing when we bring a solution to the neutral point of methyl orange, say, is to bring it to a definite hydrogen ion concentration. Therefore, if we add methyl orange to our morphine titration and bring the solution to the neutral point we are bringing the solution to a hydrogen ion concentration of about [1]PH = 4, or, if we use cochineal, to about PH = 6. Now if the hydrogen ion concentration of a solution of morphine hydrochloride of the strength used in the titration is PH = 4, methyl orange will give a correct result; if PH = 6, cochineal will give a correct result; but they cannot *both* give a correct result. It is necessary, therefore, in order to find the best indicator for use in any given titration, to determine the hydrogen ion concentration of a solution of the end product of the titration of the same strength as that produced in the titration. Then if we can find an indicator which has its color change at this hydrogen ion concentration, that indicator (other things being equal) should be the best for use in that titration.

TITRATION OF MORPHINE.

The B. P. recommends methyl orange for the titration of morphine; the U. S. P. advises cochineal. In Allen's "Commercial Organic Analysis," Vol. V, page 376, we find: "Morphine forms salts which are perfectly neutral in reaction to litmus and methyl orange, and hence it may be titrated with accuracy by the aid of standard hydrochloric acid and either of these indicators."

Experiments were therefore carried out in order to find the hydrogen ion concentration of pure morphine hydrochloride in 1 per cent. solution, which is about the strength most frequently employed in a titration.

Pure morphine was prepared from ordinary pure morphine hydrochloride by twice crystallizing from a dilute slightly alkaline solution saturated with ether. The crystals were dried and rendered anhydrous by heating at 115°.

[1] PH is the logarithm of the reciprocal of the hydrogen ion concentration in terms of normal, *i. e.*, if PH = 1 the hydrogen ion concentration is N/10. If PH = 2, N/100, etc. The lower the value of PH the more acid is the solution and *vice-versa*. At the point of absolute neutrality PH = 7.

A solution of exactly N/10 hydrochloric acid was prepared, standardized to phenolphthalein against N/10 sodium hydroxide (free from carbonate), which had been standardized against pure potassium hydrogen phthalate. In one experiment 0.817 gm. anhydrous morphine was dissolved in 28.65 cc. N/10 hydrochloric acid, and made up to 107.5 cc. with neutral distilled water (giving a 1 per cent. solution of morphine hydrochloride). The hydrogen ion concentration of this solution was determined by the colorimetric method, and found to be PH = 3.65.

The mean of several experiments gave the PH of a 1 per cent. solution of morphine hydrochloride as 3.65. Now, this figure is within the range of the color change of methyl orange, but is on the acid side of the neutral tint, that is to say, a 1 per cent. solution of morphine hydrochloride will give a decidedly pink color with methyl orange. In order to titrate morphine to methyl orange, therefore, we must finish up with a decidedly pink color. As the usual procedure in morphine titrations is to add excess of acid and titrate back with alkali, it is much more likely that the end-point taken will be on the yellow side rather than pink, and the result will be low. But methyl orange is not the best indicator for morphine titrations. If we use brom-phenol blue, an indicator which is yellow in acid solutions and blue in alkaline solutions, we find that a hydrogen ion concentration of PH = 3.65 corresponds to the first appearance of a distinct blue color when we are passing from acid to alkaline. If, therefore, we dissolve morphine in excess of standard acid and titrate back with standard alkali to brom-phenol blue until a distinct blue color appears we get a more accurate result.

With cochineal, which has a range of hydrogen ion concentration of PH = 5 to 7, it is obvious that an accurate result cannot be obtained. The results of three titrations with the three indicators may be of interest. In each case the standard solutions were standardized to the indicators used. Methyl orange was taken to its neutral orange tint:

Indicator.	*Per Cent. Morphine Found.*
Brom-phenol blue	100.0
Methyl orange	99.5
Cochineal	98.8

It may be noted that the statement frequently seen in the textbooks that a solution of morphine hydrochloride is neutral to litmus is unfounded. Pure morphine hydrochloride should be acid to litmus. Two commercial samples of morphine hydrochloride in 1 per cent. solution had a PH = 4.83 and 4.50 respectively, showing a slight excess of morphine over hydrochloric acid present. A sample of morphine crystals when titrated to the above end-point gave 101.4 per cent. morphine (hydrated), showing them to be slightly effloresced.

THE TITRATION OF QUININE.

Allen's "Commercial Organic Analysis," Vol. V, page 514, states that "Quinine is a strong base, completely neutralizing acids and forming crystallizable salts having a slight alkaline indication to litmus. Quinine also forms a series of acid salts which are neutral to methyl orange."

Squire's "Companion" states that "Quinine hydrochloride is neutral, or at the most but faintly alkaline, in reaction towards litmus paper. It is usually recommended in the textbooks to titrate quinine salts to phenolphthalein. In this way the whole of the quinine is precipitated in the course of the titration, and the end-point is not very satisfactory.

A sample of carefully purified quinine free from other cinchona alkaloids was dehydrated by heating to 120°.

0.6744 gm. anhydrous quinine was dissolved in 41.60 cc. N/10 hydrochloric acid, thus forming quinine acid hydrochloride, and diluted to 1 per cent. The PH of this solution was then determined and found as a mean of three experiments to be 3.40.

Quinine acid hydrochloride should therefore in 1 per cent. solution be neutral to brom-phenol blue, with which it should give a pale greenish-yellow color. Methyl orange would be decidedly pink at this PH.

0.7144 gm. anhydrous quinine was dissolved in 22.03 cc. N/10 hydrochloric acid and diluted to 1 per cent., forming the neutral hydrochloride. The PH of this solution was as a mean 5.15.

A solution of this PH is neutral to methyl red, with which it gives an orange color. It will be seen from the above results that we can most accurately titrate a solution of quinine hydrochloride or sulphate by adding standard acid until a pale greenish-yellow color corresponding to PH = 3.4 is obtained. A commercial sample of

quinine hydrochloride titrated in this way gave 99.79 per cent. In the same way quinine acid hydrochloride or sulphate may be titrated with standard alkali until an orange color corresponding to a PH of about 5.15 is obtained with methyl red solution. A sample of quinine acid hydrochloride titrated in this way gave 97.3 per cent. The end points are not quite so sharp with quinine as with morphine, but with a little practice quite reliable results can be obtained. This method of titration may be applied to tinct. quinin. ammon. for the combined determination of quinine and ammonia in the following manner:—25 cc. of the tincture are run into 50 cc. N/2 hydrochloric acid, brom-phenol blue is added, and the liquid titrated back with N/2 alkali until a pale greenish-yellow color is obtained. Let a = No. of cc. N/2 alkali used. Methyl red is then added to the solution and the titration continued with N/10 alkali until the pink color of the methyl red disappears and only the blue color of the brom-phenol blue remains.

Let b = No. of cc. N/10 alkali used.

W/v quinine sulphate B. P. = $b \times 0.1763$.

$$\text{W/v ammonia} = 50 - \left(a + \frac{b}{5}\right) \times 0.034.$$

Commercial samples of quinine salts tested in 1 per cent. solution gave the following values for PH:

	Ph.
Quinine hydrochloride	6.2
Quinine acid hydrochloride	3.7
Quinine acid sulphate	3.6

THE TITRATION OF ATROPINE.

The B. P. and U. S. P. employ cochineal for the titration of the alkaloids obtained from belladonna.

Squire's "Companion" (nineteenth edition) states that "atropine may be readily determined by titration, using cochineal or iodeosin as an indicator." Atropine sulphate is stated to be neutral to litmus paper.

Allen's "Commercial Organic Analysis," Vol. V, page 296, states that commercial atropine sulphate is often faintly alkaline, and keeps better when so made.

In order to determine the PH of a 1 per cent. solution of atropine hydrochloride, a known weight of pure atropine was dissolved

in the theoretical volume of N/10 hydrochloric acid and made up to 1 per cent. strength. The PH of the solution was found to be 3.75.

This corresponds to a distinct blue color with brom-phenol blue, and is reasonably close to the end-point of the morphine titration given above. It is again evident the cochineal is an unsuitable indicator for this titration, and that brom-phenol blue should be used, finishing with a distinct blue color.

A commercial sample of atropine sulphate had in 1 per cent. solution PH = 5.9, showing that it contained an excess of atropine over the sulphuric acid.

SUMMARY.

On theoretical grounds and as the result of practical experiments it has been shown that the indicators ordinarily employed for the titration of the alkaloids, morphine, quinine, and atropine, are not the most suitable for the titrations.

From measurement of the hydrogen ion concentration of the solutions of the pure hydrochlorides it was found that brom-phenol blue is a better indicator to use for morphine, atropine, and the neutral salts of quinine. For the acid salts of quinine, methyl red is the most suitable indicator.

The work for this paper was carried out in the analytical and research laboratories of Messrs. Allen and Hanburys, Ltd.

THE POLLUTION OF WATER.*

At the meeting of the American Public Health Association in San Francisco, an experienced biologist made the startling statement that if present conditions continue, the greater part of the eastern United States will be cradled in a septic tank.[1] The growing sewage pollution of our rivers and seashore has long been recognized as a problem of serious moment. There is one aspect of the subject, however, that is not generally understood. House sewage, which represents human wastes, may, of course, contain the micro-

*From *Jour. Amer. Med. Asso.*, July 30, 1921.

[1] Nelson, T. C.: Some Aspects of Pollution as Affecting Oyster Propagation, *Am. J. Pub. Health* 9:498 (June) 1921.

organisms of infectious disease and thus represent a potential menace to those who drink water or eat food that have been contaminated by it. But domestic sewage ordinarily contains nothing detrimental to the growth of the aquatic organisms which help to complete the disintegration of the excreta and which thrive on it. Sewage, indeed, supplies a source of plant and animal nutriment in the water as truly as on the soil. Nelson reminds us that under favorable conditions a small stream may dispose of the sewage of a relatively large population, and the stream in turn be supplied with a constant source of animal and plant nutriment. There is a true fertilizing action on the water, with a resultant large increase in the number of the organisms present. Since fish and shellfish utilize these plant and animal organisms as food, it follows that the addition of domestic sewage to a body of water will result ultimately in an increase in the amount of human food, in the form of fish and shellfish derived from it, as truly as though the sewage were employed in fertilizing land crops. The danger of eating shellfish removed from grossly polluted water thus lies in the presence of pathogenic bacteria, rather than in the inert organic matter present in the medium. The problem of purification of such products as oysters primarily becomes one of sanitary bacteriology. It can be met by avoiding the pollutions; or, if this is not entirely feasible, the food can still be conserved by disinfection procedures. But of late the oyster itself is becoming threatened with extinction because of an added kind of contamination represented by the great industries which discharge effluents into the streams reaching the coast. Oils, acids and alkalis, metallic poisons and other chemical compounds may interfere with all forms of life, whether micro-organisms which themselves aid in the self-purification of our natural waters, or the animals and plants which normally thrive and develop in them. In other words, the disposal of industrial wastes has complicated the disposal of human waste, and incidentally an important source of delectable human food is likely to be impaired. Something remedial must be done, and soon.

NEWS ITEMS AND PERSONAL NOTES

Dr. Alsberg Retires From U. S. Bureau of Chemistry.—Dr. Carl L. Alsberg, who has been Chief of the Bureau of Chemistry of the U. S. Department of Agriculture since 1912, has retired from that office.

He has attached himself to the Ford Research Institute of Stanford University, California, where, with other investigators working along associated lines, problems in Ford Chemistry and Nutrition will be worked out.

His place in the Bureau of Chemistry will be temporarily filled, at least, by Walter G. Campbell, who has been appointed Acting Chief. Mr. Campbell has been closely associated with the work of the Bureau since 1907, and for some time has been Assistant Chief under Dr. Alsberg.

Dr. W. W. Skinner, Chief of the Water and Beverage Laboratory since 1908, has been named Assistant Chief of the Bureau.

BOOK REVIEWS

"Bulletin of the New York Botanical Garden." By H. H. Rusby. 2:1-318. April, 1921.

This volume is a guide to the Economic Museum of the New York Botanical Garden, which has been established to furnish illustrations of useful plant products, and wherever possible, choice specimens of the plant yielding them. Dr. Rusby points out in the introduction that to a large extent, the collection represents aboriginal as well as domestic customs and uses, that the articles exhibited have positive authentication, and that at great labor and expense large amounts of material preserved for the most part in formaldehyde solutions are present in the museum for study and observation. The museum now contains 8000 articles.

It has been found convenient to group the articles in relation to their use as products, and then to subdivide these larger divisions either in the evolutionary sequence of the plants yielding them, or as in the case of foods and drugs from root to seed.

The rest of the bulletin is taken up by a comprehensive catalogue of exhibits with clear descriptive notes.

M. S. DUNN.